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AMENDMENT NO. 6 TO FORM S-1

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As filed with the Securities and Exchange Commission on July 30, 2014.

Registration No. 333-197133

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

**AMENDMENT NO. 6
TO
FORM S-1
REGISTRATION STATEMENT**

*Under
The Securities Act of 1933*

Avalanche Biotechnologies, Inc.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction of
incorporation or organization)

2836
(Primary Standard Industrial
Classification Code Number)
1035 O'Brien Drive, Suite A
Menlo Park, CA 94025
(650) 272-6269

20-5258327
(I.R.S. Employer
Identification Number)

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Thomas W. Chalberg, Jr., Ph.D.
President and Chief Executive Officer
Avalanche Biotechnologies, Inc.
1035 O'Brien Drive, Suite A
Menlo Park, CA 94025
(650) 272-6269

(Name, address, including zip code, and telephone number, including area code, of agent for service)

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Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer ☐

Non-accelerated filer ☒ (Do not check if a smaller reporting company)

Accelerated filer ☐

Smaller reporting company ☐

CALCULATION OF REGISTRATION FEE

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	AMOUNT TO BE REGISTERED ⁽¹⁾	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE PER SHARE ⁽²⁾	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE ⁽²⁾	AMOUNT OF REGISTRATION FEE
Common Stock, \$0.0001 par value per share	6,210,000	\$17.00	\$105,570,000	\$13,598 ⁽³⁾

⁽¹⁾ Includes 810,000 shares that the underwriters have the option to purchase.

⁽²⁾ Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457(a) under the Securities Act of 1933, as

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amended. Includes shares that the underwriters have the option to purchase.

- ⁽³⁾ The amount paid in connection with this filing for the aggregate registration fee of \$13,598 includes \$11,998 previously paid and \$1,600 for the additional amount of \$12,420,000 of securities included in this amendment to the registration statement.

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8 (a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting offers to buy these securities in any jurisdiction where the offer or sale is not permitted.

Subject to completion, dated July 30, 2014

PRELIMINARY PROSPECTUS



Avalanche Biotechnologies, Inc.

Common Stock

We are offering 5,400,000 shares of our common stock. This is our initial public offering and no public market currently exists for our common stock. We expect the initial public offering price to be between \$16.00 and \$17.00 per share. We have applied to list our common stock on The NASDAQ Global Market under the symbol "AAVL."

We are an "emerging growth company" as the term is used in the Jumpstart Our Business Startups Act of 2012 and, as such, we have elected to comply with certain reduced public company reporting requirements for this prospectus and future filings.

Investing in our common stock involves a high degree of risk. Please see "[Risk Factors](#)" beginning on page 11 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	PER SHARE	TOTAL
Public Offering Price	\$	\$
Underwriting Discounts and Commissions ⁽¹⁾	\$	\$
Proceeds to Avalanche Biotechnologies, Inc., before expenses	\$	\$

⁽¹⁾ The underwriters will also be reimbursed for certain expenses incurred in this offering. See "Underwriting" for details.

Regeneron Pharmaceuticals, Inc., a collaboration partner, has agreed to purchase approximately \$10.0 million of our common stock in a separate private placement concurrent with the completion of this offering at a price per share equal to the public offering price. The sale of such shares will not be registered under the Securities Act of 1933, as amended. The closing of this offering is not conditioned upon the closing of such concurrent private placement.

Certain of our existing investors have indicated an interest in purchasing an aggregate of approximately \$30.0 million of shares of the common stock in this offering on the same terms as those offered to the public. However, indications of interest are not binding agreements or commitments to purchase and any of these entities may determine to purchase more, fewer or no shares in this offering.

Delivery of the shares of common stock is expected to be made on or about _____, 2014. We have granted the underwriters an option for a period of 30 days to purchase an additional 810,000 shares of common stock. If the underwriters exercise the option in full, the total underwriting discounts and commissions payable by us will be \$ _____, and the total proceeds to us, before expenses, will be \$ _____.

Joint Book-Running Managers

Jefferies

Cowen and Company

Piper Jaffray

Co-Manager

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William Blair

Prospectus dated , 2014

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ABOUT THIS PROSPECTUS

Neither we nor the underwriters have authorized anyone to provide you with information that is different from that contained in this prospectus or in any free writing prospectus we may authorize to be delivered or made available to you. We take no responsibility for, and can provide no assurance as to the reliability of, any other information that others may give you. We and the underwriters are offering to sell shares of common stock and seeking offers to buy shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date on the front of this prospectus, regardless of the time of delivery of this prospectus or any sale of shares of our common stock.

Unless the context requires otherwise, in this prospectus the terms "Avalanche," "Avalanche Biotechnologies," "the Company," "we," "us" and "our" refer to Avalanche Biotechnologies, Inc., a Delaware corporation, unless otherwise noted.

Through and including , 2014 (the 25th day after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

Our logo and some of our trademarks and tradenames are used in this prospectus. This prospectus also includes trademarks, tradenames, and service marks that are the property of other organizations. Solely for convenience, our trademarks and tradenames referred to in this prospectus may appear without the ® and ™ symbols, but those references are not intended to indicate, in any way, that we will not assert, to the fullest extent under applicable law, our rights or the right of the applicable licensor to these trademarks and tradenames.

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PROSPECTUS SUMMARY

This summary does not contain all of the information you should consider before buying our common stock. You should read the entire prospectus carefully, especially the "Risk Factors" section beginning on page 11 and our consolidated financial statements and the related notes appearing at the end of this prospectus, before deciding to invest in our common stock.

Overview

We are a clinical-stage biotechnology company focused on discovering and developing novel gene therapies to transform the lives of patients with sight-threatening ophthalmic diseases. We have leveraged our next generation gene therapy platform, the Ocular BioFactory™, to create a robust pipeline of product candidates. Our product candidates are designed to provide long-term benefit or a functional cure for these diseases by inducing a sustained expression of a therapeutic protein with a one-time administration in the eye.

We are targeting a variety of prevalent and rare genetic ophthalmic diseases with significant unmet medical need. Set forth below is a table summarizing our development programs:

Product Candidate	Indication	Stage of Development			Near-term Milestones	Worldwide Commercial Rights
		Research	Preclinical	Phase 1 / 2		
AVA-101	Wet AMD				<ul style="list-style-type: none"> Top-line Phase 2a data expected mid-2015 IND filing 2H 2015 	Avalanche
AVA-101	DME and RVO				<ul style="list-style-type: none"> IND-enabling studies planned for 2014 and 2015 	Avalanche
AVA-201	Wet AMD (Prevention)				<ul style="list-style-type: none"> Preclinical studies in 2014 and 2015 	Avalanche
AVA-311	XLRS					Regeneron; Avalanche receives milestones and royalties and has an option to share development costs and profits

Broad Research Collaboration with Regeneron for up to 7 Additional Targets

Our lead product candidate is AVA-101 for the treatment of wet age-related macular degeneration (AMD). Standard-of-care therapies include the anti-VEGF class, which inhibit vascular endothelial growth factor (VEGF), a protein that causes abnormal blood vessel growth in wet AMD. Anti-VEGF therapies, such as Lucentis®, marketed by Genentech, Inc. and Novartis AG, and EYLEA®, marketed by Regeneron Pharmaceuticals, Inc. in the United States and Bayer HealthCare LLC outside the United States, represented over \$6.0 billion in worldwide sales in 2013, and we believe 65%-80% of those sales were for the treatment of wet AMD. Due to a variety of factors, including inconvenience and discomfort associated with frequent injections in the eye, patient compliance is a significant concern with anti-VEGF therapies. These treatments require injections every four to eight weeks to maintain efficacy and patients often experience vision loss with reduced frequency of treatment. By contrast, AVA-101 is designed to enable retinal cells to continuously produce therapeutic levels of a naturally occurring anti-VEGF protein with a single administration. Accordingly, we believe that AVA-101 could transform the treatment paradigm and address a significant unmet need in this large wet AMD market.

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We have generated human proof-of-concept data for AVA-101 in a Phase 1 trial with eight wet AMD subjects conducted at Lions Eye Institute Limited (LEI) in Australia. In that Phase 1 trial, AVA-101 was well tolerated with no drug-related adverse events. In addition, subjects treated with AVA-101 showed meaningful improvement in their visual acuity test scores (up to 15 letter improvement on an eye chart from baseline), and most subjects did not receive any rescue injections of standard-of-care therapy (required for subjects exhibiting disease progression) during the one-year trial period.

We are currently conducting a Phase 2a trial for AVA-101 at LEI with 32 additional wet AMD subjects. Interim drug safety surveillance data received in June 2014 from this ongoing study suggests that AVA-101 continues to be well tolerated. Most adverse events that have been observed to date are mild and not related to AVA-101 or the procedures used in the study. Adverse events related to study procedures include subconjunctival, vitreous and retinal hemorrhage, cataract progression and eye pain. Other infrequent adverse events may be related to study procedures, including retinal tears or holes and falls. A small number of adverse events may be possibly related to AVA-101, including inflammation and light chain analysis increase, but these were considered mild and transient and have not been associated with vision loss. We expect to receive top-line data from this ongoing Phase 2a trial in mid-2015. We own exclusive rights to develop and commercialize AVA-101 worldwide.

In addition to AVA-101, our Ocular BioFactory platform has generated other promising product candidates for the treatment of severe ocular diseases, including:

- **AVA-201 for the prevention of wet AMD.** AVA-201 produces the same anti-VEGF protein as AVA-101 using a proprietary, customized delivery mechanism, or vector, that can be administered earlier in the disease progression and before the onset of wet AMD. Up to 7.3 million patients in the United States are at high risk of developing wet AMD, and we believe that the highest risk patients can be identified through a combination of clinical and genetic biomarkers. We own exclusive rights to develop and commercialize AVA-201 worldwide.
- **AVA-311 for juvenile X-linked retinoschisis (XLRS).** AVA-311 is being developed in collaboration with our partner Regeneron for the treatment of XLRS, a rare genetic disease of the retina with no approved therapy. There are approximately 10,000 boys and young men in the United States suffering from the disease. XLRS is caused by mutation of the RS1 gene and results in splitting of retinal layers and corresponding loss of vision. Based on preclinical studies in animals to date, AVA-311 has delayed the progression of XLRS and improved vision by delivering functional copies of the RS1 gene in retinal cells of mice.

In order to accelerate the pace of generating and developing product candidates for our pipeline, we entered into a broad research collaboration and license agreement with Regeneron in May 2014. Under the terms of the collaboration, we intend to jointly discover novel product candidates based on our Ocular BioFactory platform for up to eight therapeutic targets including AVA-311. We have received an initial payment of \$8.0 million and are eligible for reimbursement of additional collaboration research costs. In addition, we are eligible to receive up to \$80.0 million in development and regulatory milestone payments for product candidates directed toward each therapeutic target, for a combined total of up to \$640 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, and low-to mid-single-digit royalties on worldwide net sales of collaboration product candidates. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits.

Our Ocular BioFactory Platform

Our Ocular BioFactory platform is designed to treat the cause of ocular diseases by enabling patients' own cells to express a therapeutic protein for a sustained period of time. We use a vector derived from adeno-associated virus (AAV), which is a small, non-pathogenic virus. DNA encoding the AAV viral genes are removed and replaced with a therapeutic gene to treat a disease. The resulting vector is used to deliver and express, or transduce, the therapeutic gene to the cells of the eye to promote continuous protein production. Although AAVs are widely used for gene therapy due to their safety, stability and sustained protein expression, our

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Ocular BioFactory platform has distinct characteristics that provide advantages over competing gene therapy technologies using AAVs as well as other viral and non-viral vectors.

Our Ocular BioFactory platform features two key proprietary components: a novel vector screening and optimization system referred to as directed evolution, and an industrialized manufacturing process. Through directed evolution, we generate a diverse library of millions of AAV variants and subsequently screen the variants in multiple *in vitro* and *in vivo* tests to identify the optimal variant for a specific disease. Our directed evolution technology allows us to create proprietary vectors and optimize them to target cells in different layers of the retina. Each of these cell layers constitutes a potential therapeutic target for currently unmet medical needs, providing us with multiple opportunities to apply our directed evolution technology. Our industrialized manufacturing process, based on our proprietary system, is highly efficient and stable. It uses the baculovirus expression system (BVES), which is a technology for producing high levels of recombinant protein in insect-derived cells. Production yields are up to one hundred times greater than those obtained using conventional AAV production systems. Therefore, we are able to manufacture commercial grade production for large markets such as wet AMD.

Experience in Ophthalmology and Gene Therapy

Our senior management team and board of directors have significant experience in the biotechnology industry, specifically in the areas of ophthalmology and gene therapy. Our Chief Executive Officer and co-founder, Thomas W. Chalberg, Jr., Ph.D., was a member of the ophthalmology team at Genentech that was responsible for the successful launch and commercialization of Lucentis. Dr. Chalberg was also a Howard Hughes Medical Institute Fellow at Stanford University, where his research focused on retinal diseases and novel technologies for gene therapy.

Our Chairman and co-founder, Mark S. Blumenkranz, M.D., is an ophthalmologist, a trained vitreoretinal surgeon and the Chairman of the Byers Eye Institute at Stanford University. Dr. Blumenkranz was also a founding member of the Eyetech scientific advisory board. Dr. Blumenkranz currently serves on the boards of directors of Vantage Surgical Systems Inc., Oculogics, Inc., Presbia Holdings, Digisight Technologies Inc. and Oculeve, Inc.

Our director and co-founder, Steven D. Schwartz, M.D., is an ophthalmologist and a trained vitreoretinal surgeon at the UCLA Jules Stein Eye Institute, where he has served as principal investigator in a number of early-stage clinical trials for retinal diseases, including the initial studies for Lucentis and novel product candidates in gene and cell therapy. Dr. Schwartz held various key positions at Eyetech, and has served on a number of scientific advisory boards, including Genentech and Ophthotech Corporation.

Other members of our executive management team also have significant experience in the discovery and development of gene therapies including expertise and/or prior experience at gene therapy companies in the following areas: regulatory, led by Samuel Barone, our Chief Medical Officer with prior experience at the Office of Cellular, Tissue and Gene Therapies at the Food and Drug Administration (FDA); manufacturing, led by Mehdi Gasmí, our Vice President, Pharmaceutical Development, with prior experience at Ceregene, Inc. and Généthron; finance, led by Linda Bain, our Chief Financial Officer with prior experience at bluebird bio, inc., Genzyme Corporation and AstraZeneca plc; and IP strategy, led by Hans Hull, our Senior Vice President, Legal and Corporate Development, with prior experience at Second Genome, Inc. and Aprelia Pharmaceuticals Company and as an attorney at Heller Ehrman White & McAulliffe LLP.

Recent Financing

In April 2014, we completed a private placement of \$55 million of shares of Series B convertible preferred stock, or the Series B Financing. Investors in the Series B Financing include, among others, Adage Capital Partners, GP, LLC, Cowen AV Investment LLC, Redmile Group, LLC, Rock Springs GP LLC, Sabby Management, LLC and entities affiliated with Deerfield Mgmt L.P. and Venrock Partners VI, L.P.

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Our goal is to transform the lives of patients suffering from blinding and sight-threatening diseases by discovering, developing and commercializing potentially curative therapies. The key elements of our strategy to achieve this goal are:

- **Successfully advance AVA-101 through clinical development and commercial launch for wet AMD.** Global sales of Lucentis and EYLEA were over \$6.0 billion in 2013 with approximately \$3.3 billion in the United States and \$2.8 billion in territories outside of the United States, of which we believe a significant portion occurred in the European Union, Japan and Australia. We believe 65%-80% of those sales were for the treatment of wet AMD. We intend to pursue a worldwide development and commercialization strategy of advancing AVA-101 in the United States and these international markets.
- **Pursue additional indications for AVA-101.** There are other diseases in which VEGF plays a central role in disease biology, including diabetic macular edema (DME) and retinal vein occlusion (RVO). Since patient compliance presents the same challenge in these indications, we believe that AVA-101 may offer an attractive alternative to the existing therapies in these markets.
- **Continue to identify and target ophthalmic diseases using our Ocular BioFactory platform.** We are focusing on both prevalent and rare ophthalmic diseases for which the disease biology is well characterized and for which the diseases themselves can be better treated by the sustained delivery of a therapeutic protein. We will continue to identify the most appropriate target indications based on emerging data from our platform, by leveraging our internal expertise and through relationships with thought leaders in ophthalmology.
- **Continue to invest in our Ocular BioFactory platform.** Our Ocular BioFactory platform has been validated by both preclinical and clinical data from our product candidates. We will continue to invest in our platform and employ directed evolution to create and manufacture vectors with higher efficiency and greater specificity that can potentially treat previously untreatable diseases.
- **Build a balanced portfolio of proprietary and partnered programs.** We plan to develop and commercialize multiple product candidates independently. For targets outside our core areas of interest or where a partner can contribute specific expertise, we intend to evaluate potential collaborations with strategic partners who can augment our industry-leading expertise in gene therapy for the eye.

Risks Associated with Our Business

Our ability to implement our business strategy is subject to numerous risks that you should be aware of before making an investment decision. These risks are described more fully in the section entitled "Risk factors" immediately following this prospectus summary. These risks include, among others:

- We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.
- If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop and commercialize AVA-101 and our other product candidates.
- Our business currently depends substantially on the success of AVA-101, which is still under development. If we are unable to obtain regulatory approval for, or successfully commercialize, AVA-101, our business will be materially harmed.
- We are conducting, and may in the future conduct, clinical trials for AVA-101 and other product candidates in sites outside the United States and the U.S. Food and Drug Administration may not accept data from trials conducted from such locations.
- Our Ocular BioFactory is based on a novel gene therapy technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. At the moment, no gene therapy products have been approved in the United States and only one gene therapy product has been approved in Europe.

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- All of our product candidates are still in preclinical or early-stage clinical development. If we are unable to commercialize our product candidates or if we experience significant delays in obtaining regulatory approval for, or commercializing, any or all of our product candidates, our business will be materially and adversely affected.
- Although AVA-101 produced in a mammalian-cell based manufacturing system is currently being evaluated in a Phase 1/2a clinical trial, neither AVA-101 manufactured in the BVES nor our other product candidates have ever been evaluated in human clinical trials.
- We rely on third parties to conduct our clinical trials. If these third parties do not meet our deadlines or otherwise conduct the trials as required, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected or at all.
- Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by other companies and universities, and unless the licensor solely owns any intellectual property it licenses to us, our licensed rights do not extend to any co-owner's undivided interest in such rights unless we also obtain a license from such co-owner. For example, The Regents of the University of California (Regents) co-own certain patent rights with Chiron Corporation (Chiron), and the Regents have licensed to us their undivided interest in these rights while Chiron retains its interest in these rights.
- Any adverse events in our clinical trials or those conducted by other parties, even if not ultimately attributable to our product candidates, or any public perception that such adverse events may occur based on claims that using virus particles to deliver gene therapy may be unsafe, could delay or halt commercialization of AVA-101 or further advancement of our clinical trials, which would have a material adverse effect on our business and operations.
- Our success depends on our ability to protect our intellectual property and our proprietary technologies.
- We have identified material weaknesses in our internal control over financial reporting which could, if not remediated, result in material misstatements in our consolidated financial statements. If we fail to maintain proper and effective internal control over financial reporting in the future, our ability to produce accurate and timely consolidated financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

Concurrent Private Placement

Upon the closing of this offering, Regeneron, a collaboration partner, has contractually agreed to purchase approximately \$10.0 million of our common stock in a concurrent private placement at a price per share equal to the public offering price. The sale of such shares will not be registered under the Securities Act of 1933, as amended (Securities Act). The closing of this offering is not conditioned upon the closing of such concurrent private placement.

Corporate Information

We were incorporated in Delaware in 2006. Our principal executive offices are located at 1035 O'Brien Drive, Suite A, Menlo Park, CA 94025, and our telephone number is (650) 272-6269. Our website address is <http://avalanchebiotech.com>. The information contained in, or that can be accessed through, our website is not part of this prospectus.

Implications of Being an Emerging Growth Company

We are an emerging growth company as defined in the Jumpstart Our Business Startups Act of 2012 (JOBS Act). We will remain an emerging growth company until the earlier of the last day of the fiscal year following the fifth anniversary of the completion of this offering, the last day of the fiscal year in which we have total annual gross revenue of at least \$1.0 billion, the last day of the fiscal year in which we are deemed to be a "large accelerated filer" as defined in Rule 12b-2 under the Securities Exchange Act of 1934, as amended (Exchange Act), which would occur if the market value of our common stock held by non-affiliates exceeded

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\$700.0 million as of the last business day of the second fiscal quarter of such fiscal year, or the date on which we have issued more than \$1.0 billion in non-convertible debt securities during the prior three-year period. An emerging growth company may take advantage of specified reduced reporting requirements and is relieved of certain other significant requirements that are otherwise generally applicable to public companies. As an emerging growth company,

- we may present only two years of audited consolidated financial statements, plus unaudited condensed consolidated financial statements for any interim period, and related management's discussion and analysis of financial condition and results of operations;
- we may avail ourselves of the exemption from the requirement to obtain an attestation and report from our auditors on the assessment of our internal control over financial reporting pursuant to the Sarbanes-Oxley Act of 2002 (Sarbanes-Oxley);
- we may provide less extensive disclosure about our executive compensation arrangements; and
- we may not require shareholder non-binding advisory votes on executive compensation or golden parachute arrangements.

However, we are choosing to "opt out" of the extended transition periods available under the JOBS Act for complying with new or revised accounting standards. Section 107 of the JOBS Act provides that our decision to opt out of the extended transition periods for complying with new or revised accounting standards is irrevocable.

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THE OFFERING	
Issuer	Avalanche Biotechnologies, Inc.
Common stock offered by us in this offering	5,400,000 shares
Common stock to be sold by us to Regeneron in the concurrent private placement	Approximately \$10.0 million (or 606,060 shares assuming a sale price of \$16.50, the midpoint of the estimated range set forth on the cover page of this prospectus)
Common stock to be outstanding after this offering and the concurrent private placement	20,775,103 shares
Use of proceeds	We estimate that the net proceeds from this offering will be approximately \$80.6 million, or approximately \$93.0 million if the underwriters exercise in full their option to purchase additional shares of common stock, at an assumed initial public offering price of \$16.50 per share, the midpoint of the estimated range set forth on the cover page of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. In addition, we will receive gross proceeds of approximately \$10.0 million from the sale of shares of common stock to Regeneron in the concurrent private placement upon the closing of this offering. We currently expect to use substantially all of our net proceeds from this offering and the concurrent private placement to fund Phase 3 research and development start up activities for our AVA-101 study to evaluate safety and efficacy in subjects with wet AMD and to fund direct Phase 1/2 research and development expenses for our other product candidates in our development program. We will use any remaining proceeds for early-stage research and development, potential future development programs, capital expenditures, working capital and other general corporate purposes. See "Use of Proceeds."
Ticker symbol on The NASDAQ Global Market	"AAVL"
<p>Certain of our existing investors have indicated an interest in purchasing an aggregate of approximately \$30.0 million of shares of the common stock in this offering on the same terms as those offered to the public. However, indications of interest are not binding agreements or commitments to purchase and any of these entities may determine to purchase more, fewer or no shares in this offering.</p> <p>In this prospectus, the number of shares of common stock to be outstanding after this offering and the concurrent private placement is based on 3,672,885 shares of common stock outstanding as of March 31, 2014, gives effect to the Transactions discussed below and excludes the following:</p> <ul style="list-style-type: none"> ▪ 4,134,200 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2014 under our Amended and Restated 2006 Equity Incentive Plan, at a weighted-average exercise price of \$0.47 per share; ▪ 105,800 shares of common stock reserved for issuance pursuant to future awards under our Amended and Restated 2006 Equity Incentive Plan as of March 31, 2014; 	

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- 2,088,332 shares of common stock reserved for issuance pursuant to future awards under our 2014 Equity Incentive Award Plan (subject to automatic annual adjustment in accordance with the terms of the plan), which will become effective immediately prior to the effectiveness of the registration statement to which this prospectus relates, of which options to purchase 455,000 shares of common stock at an exercise price equal to the initial public offering price set forth on the cover of this prospectus will be granted coincident with this offering, of which 375,000 shares will be awarded to executive officers and non-employee directors;
- 208,833 shares of common stock reserved for issuance pursuant to future awards under our 2014 Employee Stock Purchase Plan, which will become effective immediately prior to the effectiveness of the registration statement to which this prospectus relates;
- 54,716 shares of common stock issuable upon the exercise of warrants outstanding to purchase Series A convertible preferred stock as of March 31, 2014, assuming (i) cash exercise of such warrants in connection with the consummation of this offering and (ii) the conversion of the shares issuable pursuant to such warrants into common stock immediately prior to the completion of this offering, at a weighted-average exercise price of \$1.45 per share;
- 289,000 shares of common stock issuable upon the exercise of warrants outstanding to purchase common stock as of March 31, 2014, at a weighted-average exercise price of \$0.32 per share; and
- 63,415 shares of common stock issuable upon the exercise of warrants to purchase common stock that were issued in May 2014, at an exercise price of \$6.83 per share.

Except as otherwise indicated, all information contained in this prospectus (including the above discussion of the number of shares of common stock to be outstanding after this offering) assumes the following, which we refer to in this prospectus collectively as the "Transactions":

- the adoption of our amended and restated certificate of incorporation and amended and restated bylaws prior to the completion of this offering;
- the conversion of all of our outstanding shares of our convertible preferred stock into an aggregate of 10,689,027 shares of common stock, which excludes the 531,208 shares of Series A convertible preferred stock repurchased by us and includes the conversion of the 7,321,003 shares of Series B convertible preferred stock issued by us in April 2014, immediately prior to the completion of this offering;
- the issuance of 407,131 shares of our common stock upon the cash exercise of all of the warrants described above, which warrants would otherwise expire upon the completion of this offering;
- no exercise of outstanding options described above; and
- that the underwriters do not exercise their option to purchase additional shares of common stock.

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The following summary consolidated financial data for the years ended December 31, 2012 and 2013 are derived from our audited consolidated financial statements appearing elsewhere in this prospectus. The summary consolidated financial data for the three months ended March 31, 2013 and 2014, and for the period from July 17, 2006 (date of inception) to March 31, 2014 and as of March 31, 2014 are derived from our unaudited consolidated financial statements appearing elsewhere in this prospectus. The unaudited consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to present fairly our financial position as of March 31, 2014 and the results of operations for the three months ended March 31, 2013 and 2014, and for the period from July 17, 2006 (date of inception) to March 31, 2014. You should read this summary consolidated financial data together with our consolidated financial statements and related notes appearing elsewhere in this prospectus and the information under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative of our future results and interim results are not necessarily indicative of results to be expected for the full year.

(In thousands, except share and per share data)	YEARS ENDED DECEMBER 31,		THREE MONTHS ENDED MARCH 31,		PERIOD FROM JULY 17, 2006 (INCEPTION) TO MARCH 31,
	2012	2013	2013	2014	2014
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS DATA:					
Revenue:					
License revenue	\$ —	\$ —	\$ —	\$ 30	\$ 30
Government grant revenue	30	480	300	—	510
Total revenue	30	480	300	30	540
Operating expenses:					
Research and development	1,310	2,151	201	910	5,546
General and administrative	536	1,783	141	726	3,631
Total operating expenses	1,846	3,934	342	1,636	9,177
Operating loss	(1,816)	(3,454)	(42)	(1,606)	(8,637)
Interest expense, net	(8)	(73)	(13)	(14)	(114)
Other income (expense), net	7	(96)	6	(43)	(134)
Change in fair value of embedded derivative	6	18	—	—	24
Loss on extinguishment of related-party convertible notes	—	(1,671)	—	—	(1,671)
Net loss	(1,811)	(5,276)	(49)	(1,663)	(10,532)
Foreign currency translation adjustment	8	19	—	—	27
Comprehensive loss	\$ (1,803)	\$ (5,257)	\$ (49)	\$ (1,663)	\$ (10,505)
Net loss per share attributable to common stockholders—basic and diluted	\$ (0.50)	\$ (1.44)	\$ (0.01)	\$ (0.45)	
Weighted-average common shares outstanding—basic and diluted	3,642,503	3,672,885	3,672,885	3,672,885	
Pro forma net loss per share attributable to common stockholders—basic and diluted ⁽¹⁾		\$ (0.74)		\$ (0.11)	
Pro forma weighted-average common shares outstanding—basic and diluted ⁽¹⁾		6,889,774		14,741,705	

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⁽¹⁾ See Note 15 to our consolidated financial statements for an explanation of the calculations of pro-forma net loss per common share.

The table below presents our balance sheet as of March 31, 2014:

- on an actual basis;
- on a subsequent events pro forma basis to give effect to the following transactions that occurred in April 2014 that affected our cash and capitalization, as if they had occurred as of March 31, 2014: (1) the issuance of 7,025,888 shares of Series B convertible preferred stock in April 2014 in exchange for \$52.9 million in cash; (2) the conversion of \$2.0 million of principal amount of outstanding convertible notes into 295,115 shares of Series B convertible preferred stock and the related loss on extinguishment of related-party convertible notes of \$0.2 million and repurchase of beneficial conversion feature of \$2.0 million; and (3) the repurchase of 531,208 shares of Series A convertible preferred stock in April 2014 for \$4.0 million in cash;
- on a pro forma basis to give further effect to the Transactions immediately prior to the completion of this offering; and
- on a pro forma as adjusted basis to give further effect to (1) the sale of 5,400,000 shares of common stock in this offering at an assumed initial public offering price of \$16.50 per share, the midpoint of the estimated price range set forth on the cover of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, and (2) the sale of approximately \$10.0 million of shares of common stock in the concurrent private placement to Regeneron.

(In thousands)	AS OF MARCH 31, 2014			
	ACTUAL	SUBSEQUENT EVENTS PRO FORMA	PRO FORMA	PRO FORMA AS ADJUSTED ⁽¹⁾
CONSOLIDATED BALANCE SHEET DATA:				
Cash	\$ 169	\$ 50,074	\$ 50,679	\$ 141,242
Working capital	(852)	49,053	49,658	140,221
Total assets	1,103	51,008	51,613	142,176
Convertible preferred stock warrant liability	129	129	—	—
Series A convertible preferred stock	7,992	7,222	—	—
Series B convertible preferred stock	—	55,127	—	—
Deficit accumulated during the development stage	(10,532)	(13,196)	(13,196)	(13,196)
Total stockholders' equity (deficit)	(8,717)	(13,169)	49,914	140,477

⁽¹⁾ Each \$1.00 increase or decrease in the assumed initial public offering price of \$16.50 per share would increase or decrease, respectively, the amount of cash, working capital, total assets and total stockholders' equity (deficit) by approximately \$5.0 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase or decrease of 1,000,000 in the number of shares we are offering would increase or decrease, respectively, the amount of cash, working capital, total assets and stockholders' equity (deficit) by approximately \$15.3 million, assuming (i) the assumed initial public offering price per share, as set forth on the cover page of this prospectus, remains the same and (ii) the number of shares we issue and sell to Regeneron in the concurrent private placement remains the same. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

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Table of Contents**RISK FACTORS**

Investing in our common stock involves a high degree of risk. You should consider carefully the risks and uncertainties described below, together with all of the other information in this prospectus, including our consolidated financial statements and related notes included elsewhere in this prospectus, before making an investment decision. If any of the following risks are realized, our business, financial condition, results of operations and prospects could be materially and adversely affected. In that event, the trading price of our common stock could decline and you could lose part or all of your investment.

Risks Related to Our Financial Position and Need for Capital

We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.

We have incurred significant operating losses since we were founded in 2006 and expect to incur significant losses for the foreseeable future as we continue our clinical trial and development programs for AVA-101, a gene therapy product targeting vascular endothelial growth factor (VEGF) currently under development for the treatment of wet age-related macular degeneration (AMD), and our other product candidates. Our net loss for 2013 was \$5.3 million. As of March 31, 2014, we had a deficit accumulated during the development stage of \$10.5 million. Losses have resulted principally from costs incurred in our clinical trials, research and development programs and from our general and administrative expenses. In the future, we intend to continue to conduct research and development, clinical testing, regulatory compliance activities and, if AVA-101 or any of our other product candidates is approved, sales and marketing activities that, together with anticipated general and administrative expenses, will likely result in us incurring significant losses for the next several years.

We currently generate no revenue from sales, and we may never be able to commercialize AVA-101 or other future product candidates. We do not currently have the required approvals to market AVA-101 or any other future product candidates, and we may never receive them. We may not be profitable even if we or any of our future development partners succeed in commercializing any of our product candidates. Because of the numerous risks and uncertainties associated with developing and commercializing our product candidates, we are unable to predict the extent of any future losses or when we will become profitable, if at all.

If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop and commercialize AVA-101 and our other product candidates.

We will require substantial future capital in order to complete the remaining clinical development for AVA-101 and our other product candidates and to potentially commercialize these product candidates. We expect our spending levels to increase in connection with our clinical trials of AVA-101, as well as other corporate activities. The amount and timing of any expenditure needed to implement our development and commercialization programs will depend on numerous factors, including:

- the type, number, scope, progress, expansion costs, results of and timing of our planned clinical trials of AVA-101 or any of our other product candidates which we are pursuing or may choose to pursue in the future;
- the need for, and the progress, costs and results of, any additional clinical trials of AVA-101 and our other product candidates we may initiate based on the results of our planned clinical trials or discussions with the FDA, including any additional trials the FDA or other regulatory agencies may require evaluating the safety of AVA-101 and our other product candidates;
- the costs of obtaining, maintaining and enforcing our patents and other intellectual property rights;
- the costs and timing of obtaining or maintaining manufacturing for AVA-101 and our other product candidates, including commercial manufacturing if any product candidate is approved;
- the costs and timing of establishing sales and marketing capabilities and enhanced internal controls over financial reporting;
- the terms and timing of establishing collaborations, license agreements and other partnerships;
- costs associated with any new product candidates that we may develop, in-license or acquire;
- the effect of competing technological and market developments;

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- our ability to establish and maintain partnering arrangements for development; and
- the costs associated with being a public company.

Some of these factors are outside of our control. We do not expect our existing capital resources together with the net proceeds from this offering and the concurrent private placement to be sufficient to enable us to fund the completion of our clinical trials and remaining development program through commercial introduction. We expect that we will need to raise additional funds in the future.

We have not sold any products, and we do not expect to sell or derive revenue from any product sales for the foreseeable future. We may seek additional funding through collaboration agreements and public or private financings. Additional funding may not be available to us on acceptable terms or at all. In addition, the terms of any financing may adversely affect the holdings or the rights of our stockholders. In addition, the issuance of additional shares by us, or the possibility of such issuance, may cause the market price of our shares to decline.

If we are unable to obtain funding on a timely basis, we will be unable to complete the planned clinical trials for AVA-101 and our other product candidates and we may be required to significantly curtail some or all of our activities. We also could be required to seek funds through arrangements with collaborative partners or otherwise that may require us to relinquish rights to our product candidates or some of our technologies or otherwise agree to terms unfavorable to us.

Risks Related to the Discovery and Development of Our Product Candidates

Our business currently depends substantially on the success of AVA-101, which is still under development. If we are unable to obtain regulatory approval for, or successfully commercialize, AVA-101, our business will be materially harmed.

Our product candidates are in the early stage of development and will require additional preclinical studies, substantial clinical development and testing, manufacturing bridging studies and process validation and regulatory approval prior to commercialization. We have only one product candidate that has been the focus of advanced development efforts: AVA-101, a recombinant adeno-associated vector type 2 (AAV2) encoding the anti-VEGF protein sFLT-1. Successful continued development and ultimate regulatory approval of AVA-101 is critical for our future business success. We have invested, and will continue to invest, a significant portion of our time and financial resources in the development of AVA-101. We will need to raise sufficient funds for, and successfully enroll and complete, our planned clinical trials of AVA-101 in wet AMD subjects. The future regulatory and commercial success of this product candidate is subject to a number of risks, including the following:

- we may not have sufficient financial and other resources to complete the necessary clinical trials for AVA-101;
- we may not be able to provide evidence of efficacy and safety for AVA-101;
- we do not know the degree to which AVA-101 will be accepted as a therapy for wet AMD, even if approved;
- the results of our clinical trials may not meet the level of statistical or clinical significance required by the FDA or comparable foreign regulatory bodies for marketing approval;
- subjects in our clinical trials may die or suffer other adverse effects for reasons that may or may not be related to AVA-101;
- if approved for treatment of wet AMD, AVA-101 will likely compete with other treatments then available, including the off-label use of products already approved for marketing and other therapies currently available or which may be developed; and
- we may not be able to obtain, maintain or enforce our patents and other intellectual property rights.

Of the large number of biologics and drugs in development in the pharmaceutical industry, only a small percentage result in the submission of a Biologics Licensing Application (BLA) or a New Drug Application (NDA) to the FDA and even fewer are approved for commercialization. Furthermore, even if we do receive regulatory approval to market AVA-101, any such approval may be subject to limitations on the indicated uses for which we may market the product. Accordingly, even if we are able to obtain the requisite financing to continue to fund our development programs, we cannot assure you that AVA-101 will be successfully developed or commercialized. If we or any of our

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future development partners are unable to develop, or obtain regulatory approval for, or, if approved, successfully commercialize, AVA-101, we may not be able to generate sufficient revenue to continue our business.

We are conducting, and may in the future conduct, clinical trials for AVA-101 and other product candidates in sites outside the United States and the FDA may not accept data from trials conducted in such locations.

We have conducted, and may in the future choose to conduct, one or more of our clinical trials outside the United States. For example, we are currently conducting a Phase 1/2a trial for AVA-101 with LEI in Australia.

Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of this data is subject to certain conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and performed by qualified investigators in accordance with ethical principles. The study population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. Generally, the patient population for any clinical studies conducted outside of the United States must be representative of the population for whom we intend to label the product in the United States. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will be dependent upon its determination that the studies also complied with all applicable U.S. laws and regulations. There can be no assurance the FDA will accept data from trials conducted outside of the United States. If the FDA does not accept the data from our clinical trials for AVA-101 or any other product candidates, it would likely result in the need for additional trials, which would be costly and time-consuming and delay or permanently halt our development of AVA-101 or any other product candidates. The FDA may also determine that additional safety or other data are needed before we may commence a Phase 2b clinical trial which could require us to conduct additional trials before we proceed.

Our Ocular BioFactory is based on a novel gene therapy technology, which makes it difficult to predict the time and cost of product candidate development and subsequently obtaining regulatory approval. At the moment, no gene therapy products have been approved in the United States and only one gene therapy product has been approved in Europe.

We have concentrated our research and development efforts on our Ocular BioFactory, which is a gene therapy platform, and our future success depends on the successful development of product candidates based on this platform. There can be no assurance that any development problems we experience in the future related to our Ocular BioFactory platform will not cause significant delays or unanticipated costs, or that such development problems can be solved. We may also experience delays in developing a sustainable, reproducible and scalable manufacturing process or transferring that process to commercial partners, which may prevent us from completing our clinical studies or commercializing our products on a timely or profitable basis, if at all.

In addition, the clinical study requirements of the FDA, the European Medicines Agency (EMA) and other regulatory agencies and the criteria these regulators may use to determine the safety and efficacy of a product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential products. The regulatory approval process for novel product candidates such as ours can be more expensive and take longer than for other, better known or extensively studied pharmaceutical or other product candidates. As of the date of this prospectus, the FDA has not approved any gene therapy products for sale and only one gene therapy product has been approved in the Western world, which makes it difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for our product candidates in either Europe or the United States. Approvals by the EMA may not be indicative of what the FDA may require for approval.

Regulatory requirements governing gene and cell therapy products may change in the future. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within its Center for Biologics Evaluation and Research (CBER) to consolidate the review of gene therapy and related products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its review. Gene therapy clinical studies conducted at institutions that receive funding for recombinant DNA research from the U.S. National Institutes of Health (NIH) may also be subject to review by the NIH Office of Biotechnology Activities' Recombinant DNA Advisory Committee (RAC). Although the FDA decides whether individual gene therapy protocols may proceed, the RAC review process can impede the initiation of a clinical study, even if the FDA has reviewed the study and approved its initiation. Conversely, the FDA can put an Investigational New Drug application (IND) on clinical hold even if the RAC has provided a favorable review. Also, before a clinical study can begin at an NIH-funded institution, that institution's

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institutional review board (IRB) and its Institutional Biosafety Committee will have to review the proposed clinical study to assess the safety of the study. In addition, adverse developments in clinical trials of gene therapy products conducted by others may cause the FDA or other regulatory bodies to change the requirements for approval of any of our product candidates.

These regulatory review committees and advisory groups and the new guidelines they promulgate may lengthen the regulatory review process, require us to perform additional studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of these treatment candidates or lead to significant post-approval limitations or restrictions. As we advance our product candidates, we may be required to consult with these regulatory and advisory groups, and comply with applicable guidelines. If we fail to do so, we may be required to delay or discontinue development of our product candidates. Delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring a potential product to market could decrease our ability to generate sufficient product revenue to maintain our business.

All of our product candidates are still in preclinical or early-stage clinical development. If we are unable to commercialize our product candidates or if we experience significant delays in obtaining regulatory approval for, or commercializing, any or all of our product candidates, our business will be materially and adversely affected.

All of our product candidates are still in preclinical and early-stage clinical development. Our ability to generate product revenue will depend heavily on our ability to successfully develop and commercialize these product candidates. We do not expect that such commercialization of any of our product candidates will occur for at least the next several years, if ever. Our ability to commercialize our product candidates effectively will depend on several factors, including the following:

- successful completion of preclinical studies and clinical trials, including the ability to demonstrate safety and efficacy of our product candidates;
- receipt of marketing approvals from the FDA and similar regulatory authorities outside the United States;
- establishing commercial manufacturing capabilities, for example, by making arrangements with third-party manufacturers;
- successfully launching commercial sales of the product, whether alone or in collaboration with others;
- acceptance of the product by patients, the medical community and third-party payers;
- establishing market share while competing with other therapies;
- a continued acceptable safety profile of our products following regulatory approval;
- maintaining compliance with post-approval regulation and other requirements; and
- qualifying for, identifying, registering, maintaining, enforcing and defending intellectual property rights and claims covering our product candidates.

If we, or our collaborators, do not achieve one or more of these factors in a timely manner or at all, we could experience significant delays or an inability to commercialize our product candidates, which would materially and adversely affect our business, financial condition and results of operations.

We may not be successful in our efforts to identify or discover additional product candidates.

The success of our business depends primarily upon our ability to identify, develop and commercialize products based on our Ocular BioFactory platform. Although our AVA-101 product candidate is currently in clinical development, our research programs, including those subject to our collaboration with Regeneron, may fail to identify other potential product candidates for clinical development for a number of reasons. Our research methodology may be unsuccessful in identifying potential product candidates or our potential product candidates may be shown to have harmful side effects or may have other characteristics that may make the products unmarketable or unlikely to receive marketing approval.

If any of these events occur, we may be forced to abandon our development efforts for a program or programs, which would have a material adverse effect on our business and could potentially cause us to cease operations. Research programs to identify new product candidates require substantial technical, financial and human resources. We may focus our efforts and resources on potential programs or product candidates that ultimately prove to be unsuccessful.

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Drug development has inherent risk. Our lead product AVA-101 produced in mammalian-cell based manufacturing system is currently being evaluated in a Phase 1/2a human clinical trial. However, neither AVA-101 manufactured in the baculovirus expression system (BVES) system nor our other product candidates have ever been evaluated in human clinical studies, and we may experience unexpected results in the future. We or any of our future development partners will be required to demonstrate through adequate and well-controlled clinical trials that our product candidates containing our proprietary vectors are safe and effective, with a favorable benefit-risk profile, for use in their target indications before we can seek regulatory approvals for their commercial sale. Drug development is a long, expensive and uncertain process, and delay or failure can occur at any stage of development, including after commencement of any of our clinical trials.

The results of preclinical studies and early clinical trials are not always predictive of future results. Any product candidate we or any of our future development partners advance into clinical trials, including AVA-101, may not have favorable results in later clinical trials, if any, or receive regulatory approval.

If our proprietary vectors are not shown to be safe and effective in targeting retinal tissue, we may not realize the value of our investment in directed evolution technology. In addition, success in early clinical trials does not mean that later clinical trials will be successful, because product candidates in later-stage clinical trials may fail to demonstrate sufficient safety or efficacy despite having progressed through initial clinical testing. Furthermore, our future trials will need to demonstrate sufficient safety and efficacy for approval by regulatory authorities in larger patient populations. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results. In addition, only a small percentage of drugs under development result in the submission of an NDA to the FDA and even fewer are approved for commercialization.

We cannot be certain that any of our planned clinical trials will be successful, and any safety concerns observed in any one of our clinical trials in our targeted indications could limit the prospects for regulatory approval of our product candidates in those and other indications.

AVA-101 and our other product candidates are subject to extensive regulation, compliance with which is costly and time consuming, and such regulation may cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA in the United States and by comparable authorities in foreign markets. In the United States, we are not permitted to market our product candidates until we receive regulatory approval from the FDA. The process of obtaining regulatory approval is expensive, often takes many years and can vary substantially based upon the type, complexity and novelty of the products involved, as well as the target indications and patient population. Approval policies or regulations may change, and the FDA has substantial discretion in the drug approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed.

The FDA or comparable foreign regulatory authorities can delay, limit or deny approval of a product candidate for many reasons, including:

- such authorities may disagree with the design or implementation of our or any of our future development partners' clinical trials;
- we or any of our future development partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a product candidate is safe and effective for any indication;
- such authorities may not accept clinical data from trials which are conducted at clinical facilities or in countries where the standard of care is potentially different from that of the United States;
- the results of clinical trials may not demonstrate the safety or efficacy required by such authorities for approval;
- we or any of our future development partners may be unable to demonstrate that a product candidate's clinical and other benefits outweigh its safety risks;
- such authorities may disagree with our interpretation of data from preclinical studies or clinical trials;

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- approval may be granted only for indications that are significantly more limited than what we apply for and/or with other significant restrictions on distribution and use;
- such authorities may find deficiencies in the manufacturing processes or facilities of third-party manufacturers with which we or any of our future development partners contract for clinical and commercial supplies; or
- the approval policies or regulations of such authorities may significantly change in a manner rendering our or any of our future development partners' clinical data insufficient for approval.

With respect to foreign markets, approval procedures vary among countries and, in addition to the aforementioned risks, can involve additional product testing, administrative review periods and agreements with pricing authorities. In addition, events raising questions about the safety of certain marketed pharmaceuticals may result in increased cautiousness by the FDA and comparable foreign regulatory authorities in reviewing new drugs based on safety, efficacy or other regulatory considerations and may result in significant delays in obtaining regulatory approvals. Any delay in obtaining, or inability to obtain, applicable regulatory approvals would prevent us or any of our future development partners from commercializing our product candidates.

If we encounter difficulties enrolling subjects in our clinical trials, our clinical development activities could be delayed or otherwise adversely affected.

Subject enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the product candidate being studied in relation to other available therapies, including any new drugs that may be approved for the indications we are investigating. We will be required to identify and enroll a sufficient number of subjects with wet AMD for each of our planned clinical trials of AVA-101. Potential subjects for AVA-101 may not be adequately diagnosed or identified with the diseases which we are targeting or may not meet the entry criteria for our studies. We also may encounter difficulties in identifying and enrolling wet AMD subjects with a stage of disease appropriate for our planned clinical trials. In addition, we and our collaboration partner, Regeneron, are developing AVA-311 for the treatment of X-linked retinoschisis (XLRs), an orphan indication. Enrollment of eligible subjects with orphan diseases may be limited or slower than we anticipate in light of the small subject populations involved. We may not be able to initiate or continue clinical trials if we are unable to locate a sufficient number of eligible subjects to participate in the clinical trials required by the FDA or other foreign regulatory agencies. In addition, the process of finding and diagnosing subjects may prove costly.

We expect to initiate a Phase 2b clinical trial for AVA-101 in the United States in the second half of 2015. If patients are unwilling to participate in our gene therapy studies because of negative publicity from adverse events in the biotechnology or gene therapy industries or for other reasons, including competitive clinical trials for similar patient populations or available approved therapies, the timeline for recruiting subjects, conducting studies and obtaining regulatory approval of our product candidates may be delayed.

Trials using early versions of retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events. For example, generalized public backlash developed against gene therapy following the death in September 1999 of an 18-year-old who had volunteered for a gene therapy experiment at the University of Pennsylvania. Researchers at the university had infused the volunteer's liver with a gene aimed at reversing a rare metabolic disease of the liver. The procedure triggered an extreme immune-system reaction that caused multiple-organ failure in a very short time, leading to the first death to occur as a direct result of a gene therapy experiment. In addition, in 2003, 20 subjects treated for X-linked severe combined immunodeficiency in two gene therapy studies using a murine gamma-retroviral vector showed correction of the disease, but the studies were terminated after five subjects developed leukemia (four of whom were subsequently cured). The cause of these adverse events was shown to be insertional oncogenesis, which is the process whereby the corrected gene inserts near a gene that is important in a critical cellular process like growth or division, and this insertion results in the development of a cancer (often leukemia). Using molecular diagnostic techniques, it was determined that clones from these subjects showed retrovirus insertion in proximity to the promoter of the LMO2 proto-oncogene. Earlier generation retroviruses like the one used in these two studies have been shown to preferentially integrate in regulatory regions of genes that control cell growth. Our inability to enroll a sufficient number of subjects for any of

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our future clinical trials would result in significant delays or may require us to abandon one or more clinical trials altogether.

We believe we have appropriately accounted for the above factors in our trials when determining expected clinical trial timelines, but we cannot assure you that our assumptions are correct or that we will not experience delays in enrollment, which would result in the delay of completion of such trials beyond our expected timelines.

The occurrence of serious complications or side effects in connection with use of our product candidates, either in clinical trials or post-approval, could lead to discontinuation of our clinical development program, refusal of regulatory authorities to approve our product candidates or, post-approval, revocation of marketing authorizations or refusal to approve new indications, which could severely harm our business, prospects, operating results and financial condition.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries, and discomforts, to their study doctor. Often, it is not possible to determine whether or not the product candidate being studied caused these conditions. Various illnesses, injuries, and discomforts have been reported from time-to-time during clinical trials of our product candidates. It is possible that as we test our product candidates in larger, longer and more extensive clinical programs, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. Many times, side effects are only detectable after investigational products are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our product candidates has side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which would severely harm our business, prospects, operating results and financial condition.

AVA-101 is being studied in diseases of the eye in addition to AMD. There are many potential safety concerns associated with significant blockade of VEGF that may limit our ability to successfully develop and/or commercialize AVA-101. These serious and potentially life-threatening risks, based on clinical and preclinical experience of VEGF inhibitors, include bleeding, intestinal perforation, hypertension, proteinuria, congestive heart failure, heart attack, stroke and geographic atrophy. In addition, patients given infusions of any protein may develop severe hypersensitivity reactions or infusion reactions. Other VEGF inhibitors have reported side effects that became evident only after large-scale trials or after marketing approval when large numbers of patients were treated. There are risks in treating patients with gene therapy vectors, including adeno-associated virus (AAV), such as inflammation, cytotoxic T-cell response, anti-AAV antibodies and immune response to the expressed transgene, including T-cell responses and/or auto-antibodies against sFLT-1. There are risks inherent in the subretinal administration of drugs like AVA-101, which can cause injury to the eye and other complications. For example, in our Phase 1/2a trials of AVA-101 in wet AMD, the most frequent ocular adverse events to date have been subconjunctival hemorrhage, vitreous hemorrhage, cataract progression and intra-ocular inflammation.

There are also risks inherent in subretinal injections, including subretinal injections with AVA-101, such as intraocular inflammation, cataract, sterile and culture positive endophthalmitis, retinal detachment, retinal tear and other side effects. Serious complications or serious, unexpected side effects in connection with the use of AVA-101 could materially harm our business, prospects operating results and financial condition.

Risks Related to Our Reliance on Third Parties

We rely on third parties to conduct our clinical trials. If these third parties do not meet our deadlines or otherwise conduct the trials as required, our clinical development programs could be delayed or unsuccessful and we may not be able to obtain regulatory approval for or commercialize our product candidates when expected or at all.

We do not have the ability to conduct all aspects of our preclinical testing or clinical trials ourselves. We are dependent on third parties to conduct the Phase 2 and Phase 3 clinical trials for AVA-101 and preclinical and clinical trials for our other future product candidates, and, therefore, the timing of the initiation and completion of these trials is controlled by such third parties and may occur at times substantially different from our estimates. Specifically, we use clinical research organizations (CROs) to conduct our clinical trials and rely on medical institutions, clinical

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investigators, CROs and consultants to conduct our trials in accordance with our clinical protocols and regulatory requirements. Our CROs, investigators and other third parties play a significant role in the conduct of these trials and subsequent collection and analysis of data.

There is no guarantee that any CROs, investigators or other third parties on which we rely for administration and conduct of our clinical trials will devote adequate time and resources to such trials or perform as contractually required. If any of these third parties fails to meet expected deadlines, fails to adhere to our clinical protocols, fails to meet regulatory requirements, or otherwise performs in a substandard manner, our clinical trials may be extended, delayed or terminated. If any of our clinical trial sites terminates for any reason, we may experience the loss of follow-up information on subjects enrolled in our ongoing clinical trials unless we are able to transfer those subjects to another qualified clinical trial site. In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the interpretation of the study, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection of any BLA we submit by the FDA. Any such delay or rejection could prevent us from commercializing AVA-101 or our other future product candidates.

We expect to rely on third parties to conduct some or all aspects of our vector production, product manufacturing, protocol development, research and preclinical and clinical testing, and these third parties may not perform satisfactorily.

We do not expect to independently conduct all aspects of our vector production, product manufacturing, protocol development, research and preclinical and clinical testing. We currently rely, and expect to continue to rely, on third parties with respect to these items.

Any of these third parties may terminate their engagements with us at any time. If we need to enter into alternative arrangements, it could delay our product development activities. Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibility to ensure compliance with all required regulations and study protocols. For example, for product candidates that we develop and commercialize on our own, we will remain responsible for ensuring that each of our IND-enabling studies and clinical trials are conducted in accordance with the study plan and protocols.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our studies in accordance with regulatory requirements or our stated study plans and protocols, we will not be able to complete, or may be delayed in completing, the preclinical and clinical studies required to support future IND submissions and approval of our product candidates.

Reliance on third-party manufacturers entails risks to which we would not be subject if we manufactured the product candidates ourselves, including:

- the inability to negotiate manufacturing agreements with third parties under commercially reasonable terms;
- reduced control as a result of using third-party manufacturers for all aspects of manufacturing activities;
- termination or nonrenewal of manufacturing agreements with third parties in a manner or at a time that is costly or damaging to us; and
- disruptions to the operations of our third-party manufacturers or suppliers caused by conditions unrelated to our business or operations, including the bankruptcy of the manufacturer or supplier.

Any of these events could lead to clinical study delays or failure to obtain regulatory approval, or impact our ability to successfully commercialize future products.

We and our contract manufacturer are subject to significant regulation with respect to manufacturing our products. The manufacturing facility on which we rely may not continue to meet regulatory requirements and may have limited capacity.

We currently have relationships with a single supplier for the manufacturing of our viral vectors and product candidates. The supplier may require licenses to manufacture such components if such processes are not owned by the supplier or in the public domain and we may be unable to transfer or sublicense the intellectual property rights we may have with respect to such activities.

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All entities involved in the preparation of therapeutics for clinical studies or commercial sale, including our existing contract manufacturer for our product candidates, are subject to extensive regulation. Components of a finished therapeutic product approved for commercial sale or used in late-stage clinical studies must be manufactured in accordance with current Good Manufacturing Practice (cGMP). These regulations govern manufacturing processes and procedures (including record keeping) and the implementation and operation of quality systems to control and assure the quality of investigational products and products approved for sale. Poor control of production processes can lead to the introduction of adventitious agents or other contaminants, or to inadvertent changes in the properties or stability of our product candidates that may not be detectable in final product testing. We or our contract manufacturer must supply all necessary documentation in support of a BLA on a timely basis and must adhere to the FDA's current Good Laboratory Practice regulations and cGMP regulations enforced by the FDA through its facilities inspection program. Our contract manufacturer has not produced a commercially-approved product and therefore has not obtained the requisite FDA approvals to do so. Our facilities and quality systems and the facilities and quality systems of some or all of our third-party contractors must pass a pre-approval inspection for compliance with the applicable regulations as a condition of regulatory approval of our product candidates or any of our other potential products. In addition, the regulatory authorities may, at any time, audit or inspect our manufacturing facilities or those of our third-party contractors involved with the preparation of our product candidates or our other potential products or the associated quality systems for compliance with the regulations applicable to the activities being conducted. If the facility does not pass a pre-approval plant inspection, FDA approval of the products will not be granted.

The regulatory authorities also may, at any time following approval of a product for sale, audit our manufacturing facilities or those of our third-party contractors. If any such inspection or audit identifies a failure to comply with applicable regulations or if a violation of our product specifications or applicable regulations occurs independent of such an inspection or audit, we or the relevant regulatory authority may require remedial measures that may be costly and/or time-consuming for us or a third party to implement and that may include the temporary or permanent suspension of a clinical study or commercial sales or the temporary or permanent closure of a facility. Such violations could also result in civil and/or criminal penalties. Any such remedial measures or other civil and/or criminal penalties imposed upon us or third parties with whom we contract could materially harm our business.

If we or our third-party manufacturer fail to maintain regulatory compliance, the FDA can impose regulatory sanctions including, among other things, refusal to approve a pending application for a new drug product or biologic product, revocation of a pre-existing approval, other civil or criminal penalties or closing one or more manufacturing facilities. As a result, our business, financial condition and results of operations may be materially harmed.

Additionally, if supply from an approved manufacturer is interrupted, there could be a significant disruption in commercial supply. An alternative manufacturer would need to be qualified through a BLA supplement which could result in further delay. The regulatory agencies may also require additional studies if a new manufacturer is relied upon for commercial production. Switching manufacturers may involve substantial costs and is likely to result in a delay in our desired clinical and commercial timelines.

These factors could cause the delay of clinical studies, regulatory submissions, required approvals or commercialization of our product candidates, cause us to incur higher costs and prevent us from commercializing our products successfully. Furthermore, if our suppliers fail to meet contractual requirements, and we are unable to secure one or more replacement suppliers capable of production at a substantially equivalent cost, our clinical studies may be delayed or we could lose potential revenue.

Our reliance on third parties requires us to share our trade secrets, which increases the possibility that a competitor will discover them or that our trade secrets will be misappropriated or disclosed.

Because we rely on third parties to research and develop and to manufacture our product candidates, we must, at times, share trade secrets with them. We seek to protect our proprietary technology in part by entering into confidentiality agreements and, if applicable, material transfer agreements, consulting agreements or other similar agreements with our advisors, employees, third-party contractors and consultants prior to beginning research or disclosing proprietary information. These agreements typically limit the rights of the third parties to use or disclose our confidential information, including our trade secrets. Despite the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are

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disclosed or used in violation of these agreements. Given that our proprietary position is based, in part, on our know-how and trade secrets, a competitor's independent discovery of our trade secrets or other unauthorized use or disclosure would impair our competitive position and may have a material adverse effect on our business.

In addition, these agreements typically restrict the ability of our advisors, employees, third-party contractors and consultants to publish data potentially relating to our trade secrets, although our agreements may contain certain limited publication rights. For example, any academic institution that we may collaborate with in the future will usually expect to be granted rights to publish data arising out of such collaboration, provided that we are notified in advance and given the opportunity to delay publication for a limited time period in order for us to secure patent protection of intellectual property rights arising from the collaboration, in addition to the opportunity to remove confidential or trade secret information from any such publication. In the future we may also conduct joint research and development programs that may require us to share trade secrets under the terms of our research and development or similar agreements. Despite our efforts to protect our trade secrets, our competitors may discover our trade secrets, either through breach of our agreements with third parties, independent development or publication of information by any of our third-party collaborators. A competitor's discovery of our trade secrets would impair our competitive position and have an adverse impact on our business.

Risks Related to Commercialization of Our Product Candidates

Any termination or suspension of, or delays in the commencement or completion of, our planned clinical trials could result in increased costs to us, delay or limit our ability to generate revenue and adversely affect our commercial prospects.

Before we can initiate clinical trials in the United States for our product candidates, we need to submit the results of preclinical testing to the FDA, along with other information including information about product candidate chemistry, manufacturing and controls and our proposed clinical trial protocol, as part of an IND. We may rely in part on preclinical, clinical and quality data generated by CROs and other third parties for regulatory submissions for our product candidates. If these third parties do not make timely regulatory submissions for our product candidates, it will delay our plans for our clinical trials. If those third parties do not make this data available to us, we will likely have to develop all necessary preclinical and clinical data on our own, which will lead to significant delays and increase development costs of the product candidate. In addition, the FDA may require us to conduct additional preclinical testing for any product candidate before it allows us to initiate clinical testing under any IND, which may lead to additional delays and increase the costs of our preclinical development. Delays in the commencement or completion of our planned clinical trials for AVA-101 or other product candidates could significantly affect our product development costs. We do not know whether our planned trials will begin on time or be completed on schedule, if at all. The commencement and completion of clinical trials can be delayed for a number of reasons, including delays related to:

- the FDA failing to grant permission to proceed or placing the clinical trial on hold;
- subjects failing to enroll or remain in our trial at the rate we expect;
- subjects choosing an alternative treatment for the indication for which we are developing AVA-101 or other product candidates, or participating in competing clinical trials;
- lack of adequate funding to continue the clinical trial;
- subjects experiencing severe or unexpected drug-related adverse effects;
- a facility manufacturing AVA-101, any of our other product candidates or any of their components being ordered by the FDA or other government or regulatory authorities to temporarily or permanently shut down due to violations of cGMP or other applicable requirements, or infections or cross-contaminations of product candidates in the manufacturing process;
- any changes to our manufacturing process that may be necessary or desired;
- third-party clinical investigators losing the licenses or permits necessary to perform our clinical trials, not performing our clinical trials on our anticipated schedule or consistent with the clinical trial protocol, Good Clinical Practice or regulatory requirements or other third parties not performing data collection or analysis in a timely or accurate manner;
- inspections of clinical trial sites by the FDA or the finding of regulatory violations by the FDA or an IRB that require us to undertake corrective action, result in suspension or termination of one or more sites or the

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imposition of a clinical hold on the entire trial or that prohibit us from using some or all of the data in support of our marketing applications;

- third-party contractors becoming debarred or suspended or otherwise penalized by the FDA or other government or regulatory authorities for violations of regulatory requirements, in which case we may need to find a substitute contractor, and we may not be able to use some or all of the data produced by such contractors in support of our marketing applications; or
- one or more IRBs refusing to approve, suspending or terminating the trial at an investigational site, precluding enrollment of additional subjects, or withdrawing its approval of the trial.

Product development costs will increase if we have delays in testing or approval of AVA-101 or if we need to perform more or larger clinical trials than planned. Additionally, changes in regulatory requirements and policies may occur, and we may need to amend clinical trial protocols to reflect these changes. Amendments may require us to resubmit our clinical trial protocols to IRBs for reexamination, which may impact the costs, timing or successful completion of a clinical trial. If we experience delays in completion of our clinical trials, or if we, the FDA or other regulatory authorities, the IRB, other reviewing entities, or any of our clinical trial sites suspend or terminate any of our clinical trials, the commercial prospects for a product candidate may be harmed and our ability to generate product revenue will be delayed. In addition, many of the factors that cause, or lead to, termination or suspension of, or a delay in the commencement or completion of, clinical trials may also ultimately lead to the denial of regulatory approval of a product candidate. For example, if we make manufacturing or formulation changes to our product candidates, we may need to conduct additional studies to bridge our modified product candidates to earlier versions. Further, if one or more clinical trials are delayed, our competitors may be able to bring products to market before we do, and the commercial viability of AVA-101 or other product candidates could be significantly reduced.

If we do not achieve our projected development goals in the time frames we announce and expect, the commercialization of our products may be delayed and, as a result, our stock price may decline.

From time to time, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we may publicly announce the expected timing of some of these milestones. For example, throughout this prospectus, we state that we plan to begin Phase 2b trials in the second half of 2015. All of these milestones will be based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in some cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and, as a result, our stock price may decline.

Final marketing approval for AVA-101 or our other product candidates by the FDA or other regulatory authorities for commercial use may be delayed, limited or denied, any of which would adversely affect our ability to generate operating revenue.

After the completion of our clinical trials and, assuming the results of the trials are successful, the submission of a BLA, we cannot predict whether or when we will obtain regulatory approval to commercialize AVA-101 or our other product candidates, and we cannot, therefore, predict the timing of any future revenue. We cannot commercialize AVA-101 or our other product candidates until the appropriate regulatory authorities have reviewed and approved the applicable applications. We cannot assure you that the regulatory agencies will complete their review processes in a timely manner or that we will obtain regulatory approval for AVA-101 or our other product candidates. In addition, we may experience delays or rejections based upon additional government regulation from future legislation or administrative action or changes in FDA policy during the period of product development, clinical trials and FDA regulatory review. If marketing approval for AVA-101 or our other product candidates is delayed, limited or denied, our ability to market the product candidate, and our ability to generate product sales, would be adversely affected.

Even if we obtain marketing approval for AVA-101 or any other product candidate, they could be subject to restrictions or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

Even if U.S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or marketing or impose ongoing requirements for potentially costly and time consuming post-approval studies, post-market surveillance or clinical trials. Following approval, if at all, of AVA-101 or any other product

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candidates, such candidate will also be subject to ongoing FDA requirements governing the labeling, packaging, storage, distribution, safety surveillance, advertising, promotion, recordkeeping and reporting of safety and other post-market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with cGMP requirements relating to quality control, quality assurance and corresponding maintenance of records and documents. If we or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product, the manufacturing facility or us, including requesting recall or withdrawal of the product from the market or suspension of manufacturing.

If we or the manufacturing facilities for AVA-101 or any other product candidate that may receive regulatory approval, if any, fail to comply with applicable regulatory requirements, a regulatory agency may:

- issue warning letters or untitled letters;
- seek an injunction or impose civil or criminal penalties or monetary fines;
- suspend or withdraw regulatory approval;
- suspend any ongoing clinical trials;
- refuse to approve pending applications or supplements or applications filed by us;
- suspend or impose restrictions on operations, including costly new manufacturing requirements; or
- seize or detain products, refuse to permit the import or export of product or request us to initiate a product recall.

The occurrence of any event or penalty described above may inhibit our ability to commercialize our product candidates and generate revenue.

The FDA has the authority to require a risk evaluation and mitigation strategy plan as part of a BLA or NDA or after approval, which may impose further requirements or restrictions on the distribution or use of an approved drug, such as limiting prescribing to certain physicians or medical centers that have undergone specialized training, limiting treatment to patients who meet certain safe-use criteria and requiring treated patients to enroll in a registry.

In addition, if AVA-101 or any of our other product candidates is approved, our product labeling, advertising and promotion would be subject to regulatory requirements and continuing regulatory review. The FDA strictly regulates the promotional claims that may be made about prescription products. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. If we receive marketing approval for a product candidate, physicians may nevertheless prescribe it to their patients in a manner that is inconsistent with the approved label. If we are found to have promoted such off-label uses, we may become subject to significant liability. The FDA and other agencies actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant sanctions. The federal government has levied large civil and criminal fines against companies for alleged improper promotion and has enjoined several companies from engaging in off-label promotion. The FDA has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Even if we receive regulatory approval we still may not be able to successfully commercialize AVA-101 or any other product candidate, and the revenue that we generate from its sales, if any, could be limited.

Even if AVA-101 or any of our other product candidates receive regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payers or the medical community. Coverage and reimbursement of our product candidates by third-party payers, including government payers, is also generally necessary for commercial success. The degree of market acceptance of our product candidates will depend on a number of factors, including:

- demonstration of clinical efficacy and safety compared to other more-established products;
- the limitation of our targeted patient population and other limitations or warnings contained in any FDA-approved labeling;

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- acceptance of a new formulation by health care providers and their patients;
- the prevalence and severity of any adverse effects;
- new procedures or methods of treatment that may be more effective in treating or may reduce the incidences of wet AMD or other conditions for which our products are intended to treat;
- pricing and cost-effectiveness;
- the effectiveness of our or any future collaborators' sales and marketing strategies;
- our ability to obtain and maintain sufficient third-party coverage and reimbursement from government health care programs, including Medicare and Medicaid, private health insurers and other third-party payers;
- unfavorable publicity relating to the product candidate; and
- the willingness of patients to pay out-of-pocket in the absence of third-party coverage and reimbursement.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals, healthcare payers or patients, we may not generate sufficient revenue from that product candidate and may not become or remain profitable. Our efforts to educate the medical community and third-party payers on the benefits of AVA-101 or any of our other product candidates may require significant resources and may never be successful. In addition, our ability to successfully commercialize our product candidate will depend on our ability to manufacture our products, differentiate our products from competing products and defend and enforce our intellectual property rights relating to our products.

If the market for AVA-101 for the treatment of wet AMD is smaller than we believe it is, our future revenue may be adversely affected, and our business may suffer.

If the size of the market for wet AMD is smaller than we anticipate, we may not be able to achieve profitability and growth. While we are initially targeting AVA-101 for the treatment of wet AMD, a disease we believe to be the most common cause of vision loss in adults over the age of 50 in developed countries, our projections of the number of people who have wet AMD, as well as the subset of people with these diseases who have the potential to benefit from treatment with wet AMD, are based on estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations and market research and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population may be limited or may not be amenable to treatment with our product candidates, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for our product candidates, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

Coverage and reimbursement may be limited or unavailable in certain market segments for our product candidates, which could make it difficult for us to sell our product candidates profitably.

Market acceptance and sales of our product candidates will depend significantly on the availability of adequate coverage and reimbursement from third-party payers for any of our product candidates and may be affected by existing and future health care reform measures. Government authorities and third-party payers, such as private health insurers and health maintenance organizations, decide which drugs they will pay for and establish reimbursement levels. Reimbursement by a third-party payer may depend upon a number of factors including the third-party payer's determination that use of a product candidate is:

- a covered benefit under its health plan;
- safe, effective and medically necessary;
- appropriate for the specific patient;
- cost-effective; and
- neither experimental nor investigational.

Obtaining coverage and reimbursement approval for a product candidate from a government or other third-party payer is a time-consuming and costly process that could require us to provide supporting scientific, clinical and cost effectiveness

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data for the use of the applicable product candidate to the payer. We may not be able to provide data sufficient to gain acceptance with respect to coverage and reimbursement. We cannot be sure that coverage or adequate reimbursement will be available for any of our product candidates. Further, reimbursement amounts may reduce the demand for, or the price of, our product candidates. If reimbursement is not available or is available only in limited levels, we may not be able to commercialize certain of our product candidates profitably, or at all, even if approved.

As a result of legislative proposals and the trend toward managed health care in the United States, third-party payers are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. By way of example, the Medicare Prescription Drug Improvement and Modernization Act of 2003 (MMA) changed the way Medicare covers and pays for pharmaceutical products. The legislation expanded Medicare coverage for outpatient drug purchases by those covered by Medicare under a new Part D and introduced a new reimbursement methodology based on average sales prices for Medicare Part B physician-administered drugs, including drugs currently on the market used by physicians to treat wet AMD and likely AVA-101, if approved. As a result of this legislation and the expansion of federal coverage of drug products, there is additional pressure to contain and reduce costs. While the MMA applies only to drug benefits for Medicare beneficiaries, private payers often follow Medicare coverage policy and payment limitations in setting their own reimbursement rates, and any reduction in reimbursement that results from the MMA may result in a similar reduction in payments from private payers. These cost reduction initiatives and other provisions of the MMA could decrease the coverage and reimbursement that we receive for any approved products, and could seriously harm our business.

In March 2010, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively referred to as the Affordable Care Act, was enacted with a goal of reducing the cost of healthcare and substantially changing the way healthcare is financed by both government and private insurers. The Affordable Care Act, among other things, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, increased the minimum Medicaid rebates owed by manufacturers under the Medicaid Drug Rebate Program, extended the rebate program to individuals enrolled in Medicaid managed care organizations and established annual fees and taxes on manufacturers of certain prescription drugs.

Other legislative changes have also been proposed and adopted in the U.S. since the Affordable Care Act was enacted. On August 2, 2011, the Budget Control Act of 2011 created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least \$1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. This included aggregate reductions of Medicare payments to providers of 2% per fiscal year, which went into effect on April 1, 2013 and will stay in effect through 2024 unless additional Congressional action is taken.

We expect that additional healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal, state and foreign governments will pay for healthcare products and services, which could result in reduced demand for our products, if approved, or additional pricing pressures.

The continuing efforts of the government, insurance companies, managed care organizations and other payers of healthcare services to contain or reduce costs of health care may adversely affect:

- the demand for any product candidates for which we may obtain regulatory approval;
- our ability to set a price that we believe is fair for our product candidates;
- our ability to generate revenue and achieve or maintain profitability;
- the level of taxes that we are required to pay; and
- the availability of capital.

Due to the novel nature of our technology and the potential for our product candidates to offer therapeutic benefit in a single administration, we face uncertainty related to pricing and reimbursement for these product candidates.

Our product candidates are designed to provide therapeutic benefit after a single administration and, therefore, the pricing and reimbursement of our product candidates, if approved, must be adequate to support commercial

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infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell our product candidates will be adversely affected. The manner and level at which reimbursement is provided for services related to our product candidates (e.g., for administration of our product to patients) is also important. Inadequate reimbursement for such services may lead to physician resistance and adversely affect our ability to market or sell our products.

If we fail to develop and commercialize other product candidates, we may be unable to grow our business.

Although the development and commercialization of AVA-101 for the treatment of wet AMD is our primary focus, as part of our longer-term growth strategy, we plan to evaluate the development and commercialization of other therapies related to ocular diseases. We will evaluate internal opportunities from our compound libraries, and also may choose to in-license or acquire other product candidates as well as commercial products to treat patients suffering from ocular diseases such as diabetic macular edema (DME), retinal vein occlusion (RVO), glaucoma, XLRs or other disorders with high unmet medical needs and limited treatment options. These other product candidates will require additional, time-consuming development efforts prior to commercial sale, including preclinical studies, clinical trials and approval by the FDA and/or applicable foreign regulatory authorities. All product candidates are prone to the risks of failure that are inherent in pharmaceutical product development, including the possibility that the product candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure you that any such products that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective than other commercially available alternatives.

We are subject to many manufacturing risks, any of which could substantially increase our costs and limit supply of our products.

The process of manufacturing our products is complex, highly regulated and subject to several risks, including:

- The manufacturing of biologics is extremely susceptible to product loss due to contamination, equipment failure, improper installation or operation of equipment or vendor or operator error. Even minor deviations from normal manufacturing processes could result in reduced production yields, product defects and other supply disruptions. If microbial, viral or other contaminations are discovered in our products or in the manufacturing facility in which our products are made, such manufacturing facility may need to be closed for an extended period of time to investigate and remedy the contamination.
- The manufacturing facility in which our products are made could be adversely affected by equipment failures, labor shortages, contaminants, raw materials shortages, natural disasters, power failures and numerous other factors.
- We and our contract manufacturer must comply with the FDA's cGMP regulations and guidelines. We and our contract manufacturer may encounter difficulties in achieving quality control and quality assurance and may experience shortages in qualified personnel. We and our contract manufacturer are subject to inspections by the FDA and comparable agencies in other jurisdictions to confirm compliance with applicable regulatory requirements. Any failure to follow cGMP or other regulatory requirements or any delay, interruption or other issues that arise in the manufacture, fill-finish, packaging or storage of our products as a result of a failure of our facilities or the facilities or operations of third parties to comply with regulatory requirements or pass any regulatory authority inspection could significantly impair our ability to develop and commercialize our products. This may lead to significant delays in the availability of products for our clinical studies or the termination or hold on a clinical study, or the delay or prevention of a filing or approval of marketing applications for our product candidates. Significant noncompliance could also result in the imposition of sanctions, including fines, injunctions, civil penalties, failure of regulatory authorities to grant marketing approvals for our product candidates, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of products, operating restrictions and criminal prosecutions, any of which could be costly and damage our reputation. If we are not able to maintain regulatory compliance, we may not be permitted to market our products and/or may be subject to product recalls, seizures, injunctions or criminal prosecution.
- Our product candidates are biologics and require processing steps that are more complex than those required for most chemical pharmaceuticals. Moreover, unlike chemical pharmaceuticals, the physical and chemical properties of a biologic such as our product candidates generally cannot be adequately characterized prior to manufacturing the final product. As a result, an assay of the finished product is not

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sufficient to ensure that the product will perform in the intended manner. Accordingly, we expect to employ multiple steps to attempt to control our manufacturing process to assure that the process works and the product or product candidate is made strictly and consistently in compliance with the process.

- Problems with the manufacturing process, even minor deviations from the normal process, could result in product defects or manufacturing failures that result in lot failures, product recalls, product liability claims and insufficient inventory.
- Some of the raw materials required in our manufacturing process are derived from biological sources. Such raw materials are difficult to procure and may also be subject to contamination or recall. A material shortage, contamination, recall or restriction on the use of biologically derived substances in the manufacture of our product candidates could adversely impact or disrupt commercialization.
- Any adverse developments affecting manufacturing operations for our products may result in shipment delays, inventory shortages, lot failures, product withdrawals or recalls, or other interruptions in the supply of our products. We may also have to take inventory write-offs and incur other charges and expenses for products that fail to meet specifications, undertake costly remediation efforts or seek more costly manufacturing alternatives. We may encounter problems achieving adequate or clinical-grade materials that meet FDA, EMA or other applicable standards or specifications with consistent and acceptable production yields and costs.

We may not be successful in establishing and maintaining development or other strategic collaborations, which could adversely affect our ability to develop and commercialize product candidates.

We have entered into development or other strategic collaborations with major biotechnology or pharmaceutical companies. For example, our research collaboration and license agreement with Regeneron, which was announced in May 2014, covers up to eight distinct therapeutic targets, in which we could earn up to \$80.0 million in development and regulatory milestones for product candidates directed toward each therapeutic target, for a combined total of up to \$640.0 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, and low- to mid-single digit royalties on worldwide net sales of collaboration product candidates. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits.

Some of our strategic partners may terminate any agreements they enter into with us, and we may not be able to adequately protect our rights under these agreements. Furthermore, our strategic partners have negotiated for certain rights to control decisions regarding the development and commercialization of our product candidates, if approved, and may not conduct those activities in the same manner as we do.

Moreover, if we fail to maintain development or other strategic collaborations related to our product candidates that we may choose to enter into:

- the development of certain of our current or future product candidates may be terminated or delayed;
- our cash expenditures related to development of certain of our current or future product candidates would increase significantly, and we may need to seek additional financing;
- we may be required to hire additional employees or otherwise develop expertise, such as sales and marketing expertise, for which we have not budgeted; and
- we will bear all of the risk related to the development of any such product candidates.

We may form strategic alliances in the future, and we may not realize the benefits of such alliances.

We may form strategic alliances, create joint ventures or collaborations or enter into licensing arrangements with third parties that we believe will complement or augment our existing business, including for the continued development or commercialization of our product candidates. These relationships or those like them may require us to incur non-recurring and other charges, increase our near- and long-term expenditures, issue securities that dilute our existing stockholders or disrupt our management and business. In addition, we face significant competition in seeking appropriate strategic partners and the negotiation process is time-consuming and complex. Moreover, we may not be successful in our efforts to establish a strategic partnership or other alternative arrangements for AVA-101 or our other product candidates because third parties may view the risk of failure in future clinical trials as too significant or the commercial opportunity for our product candidate as too limited. We cannot be certain that, following a strategic transaction or license, we will achieve the revenue or specific net income that justifies such transaction.

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Even if we are successful in our efforts to establish development partnerships, the terms that we agree upon may not be favorable to us, and we may not be able to maintain such development partnerships if, for example, development or approval of a product candidate is delayed or sales of an approved product candidate are disappointing. Any delay in entering into development partnership agreements related to our product candidates could delay the development and commercialization of our product candidates and reduce their competitiveness if they reach the market.

If our competitors develop treatments for the target indications of our product candidates that are approved more quickly than ours, marketed more successfully or demonstrated to be safer or more effective than our product candidates, our commercial opportunity will be reduced or eliminated.

We operate in highly competitive segments of the biopharmaceutical markets. We face competition from many different sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, government agencies and private and public research institutions. Our product candidates, if successfully developed and approved, will compete with established therapies as well as with new treatments that may be introduced by our competitors. There are a variety of drug candidates in development for the indications that we intend to test. Many of our competitors have significantly greater financial, product candidate development, manufacturing and marketing resources than we do. Large pharmaceutical and biotechnology companies have extensive experience in clinical testing and obtaining regulatory approval for drugs. In addition, universities and private and public research institutes may be active in wet AMD research, and some could be in direct competition with us. We also may compete with these organizations to recruit management, scientists and clinical development personnel. We will also face competition from these third parties in establishing clinical trial sites, registering subjects for clinical trials and in identifying and in-licensing new product candidates. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

New developments, including the development of other pharmaceutical technologies and methods of treating disease, occur in the pharmaceutical and life sciences industries at a rapid pace. Developments by competitors may render our product candidates obsolete or noncompetitive. Competition in drug development is intense. We anticipate that we will face intense and increasing competition as new treatments enter the market and advanced technologies become available.

Even if we obtain regulatory approval for our product candidates, the availability and price of our competitors' products could limit the demand, and the price we are able to charge, for our product candidates. For example, EYLEA is currently available in the United States for treatment of wet AMD and macular edema following central retinal vein occlusion (CRVO), and in the United Kingdom, Germany, Switzerland, Australia, Japan and certain other countries for the treatment of wet AMD. Additionally, marketing approval has been obtained in the EU for EYLEA for the treatment of visual impairment due to macular edema secondary to CRVO. We will not achieve our business plan if the acceptance of our product candidates is inhibited by price competition or the reluctance of physicians to switch from existing methods of treatment to our product candidates, or if physicians switch to other new drug products or choose to reserve our product candidates for use in limited circumstances. Our inability to compete with existing or subsequently introduced drug products would have a material adverse impact on our business, prospects, financial condition and results of operations.

Our potential competitors in these diseases may be developing novel immune modulating therapies that may be safer or more effective than AVA-101 or our other product candidates. For example, AVA-101 will compete with a variety of therapies currently marketed and in development for wet AMD, using therapeutic modalities such as biologics, small molecules and gene therapy. Lucentis, EYLEA and Avastin® are anti-VEGF therapies that are well established and widely accepted by physicians, patients and third-party payers as the standard of care for the treatment of wet AMD. There are several other companies with marketed products or products in development for the treatment of wet AMD, including Allergan, Iconic Therapeutics, LPath, Novartis, Ocular Therapeutix, Ophthotech, Roche, Neurotech and Valeant.

Our preclinical product candidates are being developed for the treatment of prevalent or rare ophthalmic diseases, such as the prevention of wet AMD and XLRS, for which there are no approved therapies. However, there are multiple companies developing gene therapies for ophthalmic diseases, including Applied Genetic Technologies, Asklepios BioPharmaceutical Inc., Eos Neuroscience, Inc., GenSight Biologics, Genzyme Corporation, Hemera Biosciences, Inc., ReGenX Biosciences LLC, RetroSense Therapeutics, LLC and Spark Therapeutics, Inc.

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Table of Contents***We have no sales, marketing or distribution capabilities, and we may have to invest significant resources to develop these capabilities.***

We have no internal sales, marketing or distribution capabilities. If AVA-101 or any of our other product candidates ultimately receives regulatory approval, we may not be able to effectively market and distribute the product candidate. We may have to invest significant amounts of financial and management resources to develop internal sales, distribution and marketing capabilities, some of which will be committed prior to any confirmation that AVA-101 or any of our other product candidates will be approved, if at all. We may not be able to hire consultants or external service providers to assist us in sales, marketing and distribution functions on acceptable financial terms or at all. Even if we determine to perform sales, marketing and distribution functions ourselves, we could face a number of additional related risks, including:

- we may not be able to attract and build an effective marketing department or sales force;
- the cost of establishing a marketing department or sales force may exceed our available financial resources and the revenue generated by AVA-101 or any other product candidates that we may develop, in-license or acquire; and
- our direct sales and marketing efforts may not be successful.

Governments may impose price controls, which may adversely affect our future profitability.

We intend to seek approval to market our product candidates in both the United States and in foreign jurisdictions. If we obtain approval in one or more foreign jurisdictions, we will be subject to rules and regulations in those jurisdictions relating to our product candidates. In some foreign countries, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product candidate. If reimbursement of our future products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, we may be unable to achieve or sustain profitability.

Risks Related to Our Business Operations***Negative public opinion and increased regulatory scrutiny of gene therapy and genetic research may damage public perception of AVA-101 and our product candidates or adversely affect our ability to conduct our business or obtain further marketing approvals for AVA-101 and marketing approvals for our product candidates.***

Public perception may be influenced by claims that gene therapy is unsafe, and gene therapy may not gain the acceptance of the public or the medical community. In particular, our success will depend upon physicians specializing in the treatment of those diseases that our product candidates target prescribing treatments that involve the use of our product candidates in lieu of, or in addition to, existing symptomatic treatments they are already familiar with and for which greater clinical data may be available.

More restrictive government regulations or negative public opinion would have a negative effect on our business or financial condition and may delay or impair the development and commercialization of our product candidates or demand for any products we may develop. For example, in 2003, trials using early versions of murine gamma-retroviral vectors, which integrate with, and thereby alter, the host cell's DNA, have led to several well-publicized adverse events, including reported cases of leukemia. Although none of our current product candidates utilize murine gamma-retroviral vectors, our product candidates use a viral delivery system. Adverse events in our clinical trials, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public perception, potential regulatory delays in the testing or approval of our product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. Although none of our current product candidates utilize the gamma-retroviruses used in the 2003 studies, our product candidates do use a viral vector delivery system. The risk of cancer remains a concern for gene therapy and we cannot assure that it will not occur in any of our planned or future clinical studies. In addition, there is the potential risk of delayed adverse events following exposure to gene therapy products due to persistent biological activity of the genetic material or other components of products used to carry the genetic material.

Adverse events in our clinical trials or those conducted by other parties, even if not ultimately attributable to our product candidates, and the resulting publicity could result in increased governmental regulation, unfavorable public

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perception, potential regulatory delays in the testing or approval of our potential product candidates, stricter labeling requirements for those product candidates that are approved and a decrease in demand for any such product candidates. If any such adverse events occur, commercialization of AVA-101 or further advancement of our clinical trials could be halted or delayed, which would have a material adverse effect on our business and operations.

We are dependent on the services of our President and Chief Executive Officer, Thomas W. Chalberg, Jr., Ph.D., and other key executives, and if we are not able to retain these members of our management or recruit additional management, clinical and scientific personnel, our business will suffer.

We are dependent on the principal members of our management and scientific staff. The loss of service of any of our management could harm our business. In addition, we are dependent on our continued ability to attract, retain and motivate highly qualified additional management, clinical and scientific personnel. If we are not able to retain our management, particularly our President and Chief Executive Officer, Dr. Chalberg, and to attract, on acceptable terms, additional qualified personnel necessary for the continued development of our business, we may not be able to sustain our operations or grow. Although we have executed employment agreements with each member of our current executive management team, including Dr. Chalberg, these agreements are terminable at will with or without notice and, therefore, we may not be able to retain their services as expected.

We will need to expand and effectively manage our managerial, operational, financial, and other resources in order to successfully pursue our clinical development and commercialization efforts. Our success also depends on our continued ability to attract, retain and motivate highly qualified management and scientific personnel. We may not be able to attract or retain qualified management and scientific and clinical personnel in the future due to the intense competition for qualified personnel among biotechnology, pharmaceutical and other businesses, particularly in the San Francisco Bay Area. Our industry has experienced a high rate of turnover of management personnel in recent years. If we are not able to attract, retain and motivate necessary personnel to accomplish our business objectives, we may experience constraints that will significantly impede the achievement of our development objectives, our ability to raise additional capital and our ability to implement our business strategy.

Our future performance will also depend, in part, on our ability to successfully integrate newly hired executive officers into our management team and our ability to develop an effective working relationship among senior management. Our failure to integrate these individuals and create effective working relationships among them and other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates and our results of operations.

Additionally, we do not currently maintain "key person" life insurance on the lives of our executives or any of our employees. This lack of insurance means that we may not have adequate compensation for the loss of the services of these individuals.

If we fail to effectively integrate our new executive officers into our organization, the future development and commercialization of our product candidates may suffer, harming future regulatory approvals, sales of our product candidates or our results of operations.

Our current management team has only been working together for a relatively short period of time and some of our current management team have been employed by us for less than a year. Moreover, we expect to continue to expand our management team in the future. Our future performance will depend, in part, on our ability to successfully integrate recently and subsequently hired executive officers into our management team and their ability to develop and maintain an effective working relationship. Our failure to integrate these individuals with other members of management could result in inefficiencies in the development and commercialization of our product candidates, harming future regulatory approvals, sales of our product candidates and our results of operations. In addition to the competition for personnel, the San Francisco Bay Area in particular is characterized by a high cost of living. As such, we could have difficulty attracting experienced personnel to our company and may be required to expend significant financial resources in our employee recruitment and retention efforts.

We may encounter difficulties in managing our growth and expanding our operations successfully.

Because we currently have only 18 full-time employees, we will need to grow our organization substantially to continue development and pursue the potential commercialization of AVA-101 and our other product candidates, as well as function as a public company. As we seek to advance AVA-101 and other product candidates, we will need to expand our financial, development, regulatory, manufacturing, marketing and sales capabilities or contract with third

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parties to provide these capabilities for us. As our operations expand, we expect that we will need to manage additional relationships with various strategic partners, suppliers and other third parties. Future growth will impose significant added responsibilities on members of management and require us to retain additional internal capabilities. Our future financial performance and our ability to commercialize our product candidates and to compete effectively will depend, in part, on our ability to manage any future growth effectively. To that end, we must be able to manage our development efforts and clinical trials effectively and hire, train and integrate additional management, clinical and regulatory, financial, administrative and sales and marketing personnel. We may not be able to accomplish these tasks, and our failure to so accomplish could prevent us from successfully growing our company.

If we fail to comply with applicable state and federal healthcare laws, we may be subject to civil or criminal penalties and/or exclusion from federal healthcare programs.

In addition to FDA restrictions on the marketing of pharmaceutical products, several other types of state and federal healthcare fraud and abuse laws have been applied in recent years to restrict certain marketing practices in the pharmaceutical industry. These laws include anti-kickback, false claims, physician payment transparency and privacy and security laws and regulations. Because of the breadth of these laws and the narrowness of the safe harbors, it is possible that some of our business activities could be subject to challenge under one or more of these laws.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce, or in return for, purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid or other federally financed healthcare programs. Remuneration has been broadly defined to include anything of value, including cash, improper discounts, and free or reduced price items and services. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formula managers on the other. Although there are several statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchasing or recommending may be subject to scrutiny if they do not qualify for an exemption or safe harbor. Many states have similar laws that apply to their state health care programs as well as private payers.

The federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) created new federal criminal statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payers, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. The Affordable Care Act, among other things, amended the intent requirement of the federal Anti-Kickback Statute and certain criminal statute governing healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the Affordable Care Act provided that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Additionally, the False Claims Act prohibits knowingly presenting or causing the presentation of a false, fictitious or fraudulent claim for payment to the U.S. government. Actions under the False Claims Act may be brought by the Attorney General or as a qui tam action by a private individual in the name of the government. Violations of the False Claims Act can result in significant monetary penalties and treble damages. The federal government is using the False Claims Act, and the accompanying threat of significant liability, in its investigation and prosecution of pharmaceutical and biotechnology companies throughout the country, for example, in connection with the promotion of products for unapproved uses and other sales and marketing practices. The government has obtained multi-million and multi-billion dollar settlements under the False Claims Act in addition to individual criminal convictions under applicable criminal statutes. Given the significant size of actual and potential settlements, it is expected that the government will continue to devote substantial resources to investigating healthcare providers' and manufacturers' compliance with applicable fraud and abuse laws.

In addition, there has been a recent trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The Affordable Care Act, among other things, imposes new reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members. Failure to submit required information

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may result in civil monetary penalties of up to an aggregate of \$150,000 per year (or up to an aggregate of \$1 million per year for "knowing failures"), for all payments, transfers of value or ownership or investment interests that are not timely, accurately and completely reported in an annual submission. The period between August 1, 2013 and December 31, 2013 was the first reporting period, and manufacturers were required to report aggregate payment data by March 31, 2014, and to report detailed payment data and submit legal attestation to the accuracy of such data by June 30, 2014. Thereafter, manufacturers must submit reports by the 90th day of each subsequent calendar year. Certain states also mandate implementation of commercial compliance programs, impose restrictions on drug manufacturer marketing practices and/or require the tracking and reporting of gifts, compensation and other remuneration to physicians.

In the course of conducting our business, we may also obtain certain confidential patient health information including retinal scans from subjects participating in our clinical trials. In the event of an inadvertent disclosure or security breach, we could be subject to enforcement measures, including civil and criminal penalties and fines for violations of state and federal privacy or security standards, such as HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009 (HITECH), and their respective implementing regulations, including the final omnibus rule published on January 25, 2013. Additionally, certain states have adopted comparable privacy and security laws and regulations, some of which may be more stringent than HIPAA. HIPAA, HITECH and comparable state laws and regulations will be subject to interpretation by various courts and other governmental authorities, thus creating potentially complex compliance issues for us and our future customers and strategic partners. Any liability from failure to comply with the requirements of these laws, to the extent such requirements are deemed to apply to our operations, could adversely affect our financial condition. The costs of complying with privacy and security related legal and regulatory requirements are burdensome and could have a material adverse effect on our results of operations.

The need to build and maintain a robust compliance program with different compliance and/or reporting requirements increases the possibility that a healthcare company may violate one or more of the requirements. If our operations are found to be in violation of any of such laws or any other governmental regulations that apply to us, we may be subject to penalties, including, without limitation, civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and our financial results.

We and our development partners, third-party manufacturer and suppliers use biological materials and may use hazardous materials, and any claims relating to improper handling, storage or disposal of these materials could be time consuming or costly.

We and our development partners, third-party manufacturer and suppliers may use hazardous materials, including chemicals and biological agents and compounds that could be dangerous to human health and safety or the environment. Our operations and the operations of our third-party manufacturers and suppliers also produce hazardous waste products. Federal, state and local laws and regulations govern the use, generation, manufacture, storage, handling and disposal of these materials and wastes. Compliance with applicable environmental laws and regulations may be expensive, and current or future environmental laws and regulations may impair our product development efforts. In addition, we cannot entirely eliminate the risk of accidental injury or contamination from these materials or wastes. We do not carry specific biological or hazardous waste insurance coverage, and our property, casualty and general liability insurance policies specifically exclude coverage for damages and fines arising from biological or hazardous waste exposure or contamination. Accordingly, in the event of contamination or injury, we could be held liable for damages or be penalized with fines in an amount exceeding our resources, and our clinical trials or regulatory approvals could be suspended.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of AVA-101 or our other product candidates.

We face an inherent risk of product liability as a result of the clinical testing of AVA-101 and our other product candidates and will face an even greater risk if we commercialize our product candidates. For example, we may be sued if AVA-101 or our other product candidates allegedly cause injury or are found to be otherwise unsuitable during product testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the product candidate, negligence, strict liability and a breach of warranties. Claims could also be asserted under state consumer protection acts.

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If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or cease the commercialization of our product candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for AVA-101 or our other product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs to defend the related litigation;
- a diversion of management's time and our resources;
- substantial monetary awards to trial participants or patients;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- the inability to commercialize AVA-101 or our other product candidates; and
- a decline in our stock price.

We do not currently maintain product liability insurance. However, we are named as a beneficiary on the product liability insurance policy maintained by one trial sponsors, with up to \$10.0 million in coverage as a beneficiary under such policy. In the future, we plan to obtain additional product liability insurance coverage in an amount and on terms and conditions that are customary for similarly situated companies and that are satisfactory to our board of directors. Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of AVA-101 or our other product candidates. Although we plan to maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. Our insurance policies will also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We may have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

We and any of our future development partners will be required to report to regulatory authorities if any of our approved products cause or contribute to adverse medical events, and any failure to do so would result in sanctions that would materially harm our business.

If we and any of our future development partners or CROs are successful in commercializing our products, the FDA and foreign regulatory authorities would require that we and any of our future development partners report certain information about adverse medical events if those products may have caused or contributed to those adverse events. The timing of our obligation to report would be triggered by the date we become aware of the adverse event as well as the nature of the event. We and any of our future development partners may fail to report adverse events we become aware of within the prescribed timeframe. We and any of our future development partners may also fail to appreciate that we have become aware of a reportable adverse event, especially if it is not reported to us as an adverse event or if it is an adverse event that is unexpected or removed in time from the use of our products. If we and any of our future development partners fail to comply with our reporting obligations, the FDA or a foreign regulatory authority could take action, including criminal prosecution, the imposition of civil monetary penalties, seizure of our products or delay in approval or clearance of future products.

Our internal computer systems, or those of our development partners, third-party clinical research organizations or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Despite the implementation of security measures, our internal computer systems and those of our current and any future CROs and other contractors, consultants and collaborators are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. While we have not experienced any such material system failure, accident or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other similar disruptions. For example, the loss of

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clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Likewise, we rely on third parties to manufacture our product candidates and conduct clinical trials, and similar events relating to their computer systems could also have a material adverse effect on our business. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability and the further development and commercialization of our product candidate could be delayed.

Business disruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics and other natural or manmade disasters or business interruptions, for which we are predominantly self-insured. We rely on third-party manufacturers to produce AVA-101 and our other product candidates. Our ability to obtain clinical supplies of AVA-101 or our other product candidates could be disrupted if the operations of these suppliers are affected by a man-made or natural disaster or other business interruption. The occurrence of any of these business disruptions could seriously harm our operations and financial condition and increase our costs and expenses.

Our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, CROs, consultants and vendors may engage in fraudulent conduct or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or disclosure of unauthorized activities to us that violates: (1) FDA regulations, including those laws requiring the reporting of true, complete and accurate information to regulatory authorities, (2) manufacturing standards, (3) federal and state health care fraud and abuse laws and regulations or (4) laws that require the reporting of financial information or data accurately. Specifically, sales, marketing, and business arrangements in the health care industry are subject to extensive laws and regulations intended to prevent fraud, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Activities subject to these laws also involve improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. It is not always possible to identify and deter misconduct by employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of civil, criminal and administrative penalties, damages, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, and curtailment of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

Risks Relating to Our Intellectual Property***Our rights to develop and commercialize our product candidates are subject in part to the terms and conditions of licenses granted to us by other companies and universities.***

We currently are heavily reliant upon licenses of certain patent rights and proprietary technology from third parties that is important or necessary to the development of our technology and products, including technology related to our manufacturing process and our gene therapy product candidates. These and other licenses may not provide adequate rights to use such intellectual property and technology in all relevant fields of use and in all territories in which we may wish to develop or commercialize our technology and products in the future. For example, the license granted to us by the Regents to make, have made, use, offer for sale, import, export and sell products covered by certain patent rights licensed to us under our agreement with the Regents is limited to the United States. The license is also limited to the Regents' interest in the licensed patent rights which are co-owned by Chiron. As a result, we may not be able to prevent competitors from developing and commercializing competitive products in territories not included in our licenses to patents.

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Licenses to additional third-party technology that may be required for our development programs may not be available in the future or may not be available on commercially reasonable terms, which could have a material adverse effect on our business and financial condition.

In some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain the patents, covering technology that we license from third parties. In addition, we must obtain consent from the Regents before we can enforce patent rights licensed to us by the Regents. While such consent may not be unreasonably withheld, the Regents may withhold such consent or may not provide it on a timely basis. Therefore, we cannot be certain that these patents and applications will be prosecuted and enforced in a manner consistent with the best interests of our business. In addition, if third parties who license patents to us fail to maintain such patents, or lose rights to those patents, the rights we have licensed may be reduced or eliminated.

The patent rights subject to our exclusive license with the Regents are jointly owned by Chiron Corporation.

We currently have a license to the Regents' undivided interest in certain patent rights relating to the use of recombinant gene delivery vectors for treating or preventing diseases of the eye. The licensed patent rights are jointly owned by the Regents and Chiron but our license extends only the Regents' interest in such patent rights. As a result, Chiron has a right to develop and commercialize products and technology using these patent rights, and to license to third parties the right to do so. This may lead to the development and commercialization of products and technology by others that are based on technology similar to our Ocular BioFactory platform, which may impair our competitive position in the marketplace and have an adverse impact on our business.

Joint ownership of these patent rights may also limit our ability to effectively enforce our rights in these patents against alleged infringers. First, Chiron may be required to participate in any potential suit against such third party infringers but may not agree to do so. Additionally, Chiron may choose to license its interest in these patent rights to any such infringers without our consent in certain countries. Further, Chiron's joint ownership may limit the Regents' ability to prosecute related patent rights in foreign jurisdictions without the cooperation of Chiron. As a result, our business may be adversely impaired.

Our success depends on our ability to protect our intellectual property and our proprietary technologies.

Our commercial success depends in part on our ability to obtain and maintain patent protection and trade secret protection for our product candidates, proprietary technologies, and their uses as well as our ability to operate without infringing upon the proprietary rights of others. There can be no assurance that our patent applications or those of our licensors will result in additional patents being issued or that issued patents will afford sufficient protection against competitors with similar technology, nor can there be any assurance that the patents issued will not be infringed, designed around or invalidated by third parties. Even issued patents may later be found unenforceable or may be modified or revoked in proceedings instituted by third parties before various patent offices or in courts. The degree of future protection for our proprietary rights is uncertain. Only limited protection may be available and may not adequately protect our rights or permit us to gain or keep any competitive advantage. This failure to properly protect the intellectual property rights relating to our product candidates could have a material adverse effect on our financial condition and results of operations.

Composition-of-matter patents on the biological or chemical active pharmaceutical ingredient are generally considered to be the strongest form of intellectual property protection for pharmaceutical products, as such patents provide protection without regard to any method of use. While we have an issued composition-of-matter patent in the United States for AVA-101, we cannot be certain that the claims in our patent applications covering composition-of-matter of our other product candidates will be considered patentable by the United States Patent and Trademark Office (USPTO) and courts in the United States or by the patent offices and courts in foreign countries, nor can we be certain that the claims in our issued composition-of-matter patents will not be found invalid or unenforceable if challenged.

In addition to our composition of matter patent and applications, we have an issued method-of-use patent in the United States that encompasses AVA-101. Method-of-use patents protect the use of a product for the specified method or for treatment of a particular indication. However, this type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products "off-label." Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent or prosecute.

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The patent application process is subject to numerous risks and uncertainties, and there can be no assurance that we or any of our future development partners will be successful in protecting our product candidates by obtaining and defending patents. These risks and uncertainties include the following:

- the USPTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other provisions during the patent process. There are situations in which noncompliance can result in abandonment or lapse of a patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. In such an event, competitors might be able to enter the market earlier than would otherwise have been the case;
- patent applications may not result in any patents being issued;
- patents that may be issued or in-licensed may be challenged, invalidated, modified, revoked, circumvented, found to be unenforceable or otherwise may not provide any competitive advantage;
- our competitors, many of whom have substantially greater resources than we do and many of whom have made significant investments in competing technologies, may seek or may have already obtained patents that will limit, interfere with or eliminate our ability to make, use, and sell our potential product candidates;
- there may be significant pressure on the U.S. government and international governmental bodies to limit the scope of patent protection both inside and outside the United States for disease treatments that prove successful, as a matter of public policy regarding worldwide health concerns; and
- countries other than the United States may have patent laws less favorable to patentees than those upheld by United States courts, allowing foreign competitors a better opportunity to create, develop and market competing product candidates.

In addition, we rely on the protection of our trade secrets and proprietary know-how. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties, and confidential information and inventions agreements with employees, consultants and advisors, we cannot provide any assurances that all such agreements have been duly executed, and third parties may still obtain this information or may come upon this or similar information independently. Additionally, if the steps taken to maintain our trade secrets are deemed inadequate, we may have insufficient recourse against third parties for misappropriating our trade secrets. If any of these events occurs or if we otherwise lose protection for our trade secrets or proprietary know-how, the value of this information may be greatly reduced.

Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our developmental and commercialization efforts.

The biotechnology industry has been characterized by frequent litigation regarding patent and other intellectual property rights. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing product candidates. As the biotechnology industry expands and more patents are issued, the risk increases that our product candidates may be subject to claims of infringement of the patent rights of third parties. Because patent applications are maintained in secrecy until the application is published, we may be unaware of third party patents that may be infringed by commercialization of AVA-101 or our other product candidates. Moreover, because patent applications can take many years to issue, there may be currently-pending patent applications that may later result in issued patents that our product candidates may infringe. In addition, identification of third party patent rights that may be relevant to our technology is difficult because patent searching is imperfect due to differences in terminology among patents, incomplete databases and the difficulty in assessing the meaning of patent claims. Any claims of patent infringement asserted by third parties would be time consuming and could:

- result in costly litigation;
- divert the time and attention of our technical personnel and management;
- cause development delays;
- prevent us from commercializing AVA-101 or our other product candidates until the asserted patent expires or is held finally invalid or not infringing in a court of law;
- require us to develop non-infringing technology, which may not be possible on a cost-effective basis; or
- require us to enter into royalty or licensing agreements, which may not be available on commercially reasonable terms, or at all.

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Although no third party has asserted a claim of patent infringement against us as of the date of this prospectus, others may hold proprietary rights that could prevent AVA-101 or our other product candidates from being marketed. Any patent-related legal action against us claiming damages and seeking to enjoin commercial activities relating to our product candidate or processes could subject us to potential liability for damages and require us to obtain a license to continue to manufacture or market AVA-101 or our other product candidates. We cannot predict whether we would prevail in any such actions or that any license required under any of these patents would be made available on commercially acceptable terms, if at all. In addition, we cannot be sure that we could redesign our product candidate or processes to avoid infringement, if necessary. Accordingly, an adverse determination in a judicial or administrative proceeding, or the failure to obtain necessary licenses, could prevent us from developing and commercializing AVA-101 or our other product candidates, which could harm our business, financial condition and operating results.

The patent protection and patent prosecution for some of our product candidates may be dependent on third parties.

While we normally seek to obtain the right to control the prosecution and maintenance of the patents relating to our product candidates, there may be times when the filing and prosecution activities for platform technology patents that relate to our product candidates are controlled by our licensors. For example, we do not have the right to prosecute and maintain the patent rights licensed to us under agreements with each of the Regents and Virovek Corporation, and our ability to have input into such filing and prosecution activities is limited. If these licensors or any of our future licensors fail to appropriately prosecute and maintain patent protection for patents covering any of our product candidates or companion diagnostic, our ability to develop and commercialize those product candidates and companion diagnostic may be adversely affected and we may not be able to prevent competitors from making, using and selling competing products.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming, and unsuccessful. Further, our issued patents could be found invalid or unenforceable if challenged in court.

If we or any of our future development partners were to initiate legal proceedings against a third party to enforce a patent directed at one of our product candidates, or one of our future product candidates, the defendant could counterclaim that our patent is invalid and/or unenforceable in whole or in part. In patent litigation in the United States, defendant counterclaims alleging invalidity and/or unenforceability are commonplace. Grounds for a validity challenge include an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness or non-enablement. Grounds for an unenforceability assertion could include an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO or made a misleading statement during prosecution. Third parties may also raise similar claims before the USPTO, even outside the context of litigation. The outcome following legal assertions of invalidity and unenforceability is unpredictable. With respect to the validity question, for example, we cannot be certain that there is no invalidating prior art of which we and the patent examiner were unaware during prosecution. If a defendant were to prevail on a legal assertion of invalidity and/or unenforceability, we would lose at least part, and perhaps all, of the patent protection on such product candidate. Such a loss of patent protection would have a material adverse impact on our business.

Interference proceedings provoked by third parties or brought by us or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development or manufacturing partnerships that would help us bring our product candidates to market.

Even if resolved in our favor, litigation or other legal proceedings relating to our intellectual property rights may cause us to incur significant expenses, and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our ordinary shares. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any

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future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could compromise our ability to compete in the marketplace.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions, or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our common stock.

Recent patent reform legislation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents.

On September 16, 2011, the Leahy-Smith America Invents Act (Leahy-Smith Act), was signed into law. The Leahy-Smith Act includes a number of significant changes to U.S. patent law. These include provisions that affect the way patent applications will be prosecuted and may also affect patent litigation. In particular, under the Leahy-Smith Act, the United States transitioned in March 2013 to a "first to file" system in which the first inventor to file a patent application will be entitled to the patent. Third parties are allowed to submit prior art before the issuance of a patent by the USPTO, and may become involved in post-grant proceedings including opposition, derivation, reexamination, inter-partes review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope or enforceability of, or invalidate, our patent rights, which could adversely affect our competitive position.

We may not be successful in obtaining or maintaining necessary rights to our product candidates through acquisitions and in-licenses.

We currently have rights to the intellectual property, through licenses from third parties and under patents that we own, to develop our product candidates. Because our programs may require the use of proprietary rights held by third parties, the growth of our business will likely depend in part on our ability to acquire, in-license, or use these proprietary rights. For example, our product candidates may require specific formulations to work effectively and efficiently and the rights to these formulations may be held by others. We may be unable to acquire or in-license any compositions, methods of use, processes, or other third-party intellectual property rights from third parties that we identify as necessary for our product candidates. The licensing and acquisition of third-party intellectual property rights is a competitive area, and a number of more established companies are also pursuing strategies to license or acquire third-party intellectual property rights that we may consider attractive. These established companies may have a competitive advantage over us due to their size, cash resources, and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. We also may be unable to license or acquire third-party intellectual property rights on terms that would allow us to make an appropriate return on our investment.

We sometimes collaborate with U.S. and foreign academic institutions to accelerate our preclinical research or development under written agreements with these institutions. Typically, these institutions provide us with an option to negotiate a license to any of the institution's rights in technology resulting from the collaboration. Regardless of such option, we may be unable to negotiate a license within the specified timeframe or under terms that are acceptable to us. If we are unable to do so, the institution may offer the intellectual property rights to other parties, potentially blocking our ability to pursue our program.

If we are unable to successfully obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may have to abandon development of that program and our business and financial condition could suffer.

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We may fail to comply with any of our obligations under existing agreements pursuant to which we license or have otherwise acquired intellectual property rights or technology, which could result in the loss of rights or technology that are material to our business.

Licensing of intellectual property is of critical importance to our business and involves complex legal, business, and scientific issues. Disputes may arise regarding our rights to intellectual property licensed to us from a third party, including but not limited to:

- the scope of rights granted under the license agreement and other interpretation-related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the ownership of inventions and know-how resulting from the creation or use of intellectual property by us, alone or with our licensors and collaborators;
- the scope and duration of our payment obligations;
- our rights upon termination of such agreement; and
- the scope and duration of exclusivity obligations of each party to the agreement.

If disputes over intellectual property and other rights that we have licensed or acquired from third parties prevent or impair our ability to maintain our current licensing arrangements on acceptable terms, we may be unable to successfully develop and commercialize the affected product candidates.

We may be subject to claims that we have wrongfully hired an employee from a competitor or that we or our employees have wrongfully used or disclosed alleged confidential information or trade secrets of their former employers.

As is common in the biotechnology and pharmaceutical industry, in addition to our employees, we engage the services of consultants to assist us in the development of our product candidates. Many of these employees and consultants, and many of our employees, were previously employed at, or may have previously provided or may be currently providing consulting services to, other biotechnology or pharmaceutical companies including our competitors or potential competitors. We may become subject to claims that our company, our employees or a consultant inadvertently or otherwise used or disclosed trade secrets or other information proprietary to their former employers or their former or current clients. Litigation may be necessary to defend against these claims. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could adversely impact our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to our management team.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We may also be subject to claims that former employees, collaborators or other third parties have an ownership interest in our patents or other intellectual property. We may be subject to ownership disputes in the future arising, for example, from conflicting obligations of consultants or others who are involved in developing our product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or ownership. If we fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, valuable intellectual property. Such an outcome could have a material adverse effect on our business. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees.

If we do not obtain patent term extension and data exclusivity for our product candidates, our business may be materially harmed.

Depending upon the timing, duration and specifics of FDA marketing approval of AVA-101 or other product candidates, one or more of our United States patents may be eligible for limited patent term restoration under the Drug Price Competition and Patent Term Restoration Act of 1984 (Hatch-Waxman Amendments). The Hatch-Waxman Amendments permit a patent restoration term of up to five years as compensation for patent term lost during product development and the FDA regulatory review process. However, we may not be granted an extension because of, for example, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant

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patents or otherwise failing to satisfy applicable requirements. Moreover, the applicable time period or the scope of patent protection afforded could be less than we request. If we are unable to obtain patent term extension or restoration or the term of any such extension is less than we request, our competitors may obtain approval of competing products following our patent expiration, and our revenue could be reduced, possibly materially.

If our trademarks and trade names are not adequately protected, then we may not be able to build name recognition in our markets of interest and our business may be adversely affected.

Our registered or unregistered trademarks or trade names may be challenged, infringed, circumvented or declared generic or determined to be infringing on other marks. We may not be able to protect our rights to these trademarks and trade names, which we need to build name recognition among potential partners or customers in our markets of interest. At times, competitors may adopt trade names or trademarks similar to ours, thereby impeding our ability to build brand identity and possibly leading to market confusion. In addition, there could be potential trade name or trademark infringement claims brought by owners of other registered trademarks or trademarks that incorporate variations of our registered or unregistered trademarks or trade names. Over the long term, if we are unable to establish name recognition based on our trademarks and trade names, then we may not be able to compete effectively and our business may be adversely affected. Our efforts to enforce or protect our proprietary rights related to trademarks, trade secrets, domain names, copyrights or other intellectual property may be ineffective and could result in substantial costs and diversion of resources and could adversely impact our financial condition or results of operations.

Changes in U.S. patent law could diminish the value of patents in general, thereby impairing our ability to protect our product candidates.

As is the case with other biopharmaceutical companies, our success is heavily dependent on intellectual property, particularly patents. Obtaining and enforcing patents in the biopharmaceutical industry involve a high degree of technological and legal complexity. Therefore, obtaining and enforcing biopharmaceutical patents is costly, time consuming and inherently uncertain. In addition, Congress may pass patent reform legislation that is unfavorable to us. The Supreme Court has ruled on several patent cases in recent years, either narrowing the scope of patent protection available in certain circumstances or weakening the rights of patent owners in certain situations. In addition to increasing uncertainty with regard to our ability to obtain patents in the future, this combination of events has created uncertainty with respect to the value of patents, once obtained. Depending on decisions by the United States Congress, the federal courts and the USPTO, the laws and regulations governing patents could change in unpredictable ways that would weaken our ability to obtain new patents or to enforce our existing patents and patents we might obtain in the future.

We may not be able to protect our intellectual property rights throughout the world.

While we have issued patents directed at AVA-101 in the United States and pending patent applications directed at AVA-101 and other product candidates in the United States and other countries, filing, prosecuting and defending patents on AVA-101 and our other product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States can be less extensive than those in the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection but enforcement is not as strong as that in the United States. These products may compete with our product candidates, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents and other intellectual property protection, particularly those relating to biopharmaceuticals, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages

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or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Intellectual property rights do not necessarily address all potential threats to our competitive advantage.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations, and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make gene therapies that are similar to our product candidates but that are not covered by the claims of the patents that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to make the inventions covered by the issued patent or pending patent application that we own or have exclusively licensed;
- we or our licensors or future collaborators might not have been the first to file patent applications covering certain of our inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our intellectual property rights;
- it is possible that our pending patent applications will not lead to issued patents;
- issued patents that we own or have exclusively licensed may be held invalid or unenforceable, as a result of legal challenges by our competitors;
- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Should any of these events occur, they could significantly harm our business, results of operations and prospects.

Risks Related to Our Common Stock and this Offering

We have identified material weaknesses in our internal control over financial reporting which could, if not remediated, result in material misstatements in our consolidated financial statements. If we fail to maintain proper and effective internal control over financial reporting in the future, our ability to produce accurate and timely consolidated financial statements could be impaired, which could harm our operating results, investors' views of us and, as a result, the value of our common stock.

In connection with the preparation of our consolidated financial statements included in this prospectus and registration statement, we determined that we had a material weakness in our internal control over financial reporting as of December 31, 2012 and 2013 relating to the design and operation of our control environment. A material weakness is a deficiency, or a combination of deficiencies, in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of the company's annual or interim consolidated financial statements will not be prevented or detected on a timely basis. We did not maintain an effective control environment, which is the foundation for effective internal control over financial reporting, as evidenced by: (i) an insufficient number of personnel to perform control monitoring activities, (ii) an insufficient number of personnel with an appropriate level of GAAP knowledge, (iii) insufficient corporate involvement to identify and resolve errors in recording transactions and (iv) inadequate processes for the preparation and review of our consolidated financial statements. In order to remediate this material weakness, we have hired an experienced Chief Financial Officer and Corporate Controller; we are actively seeking additional accounting and finance staff members to augment our current staff and we are formalizing our accounting policies and internal controls documentation and strengthening supervisory reviews by our management.

Pursuant to Section 404 of Sarbanes-Oxley, our management will be required to report upon the effectiveness of our internal control over financial reporting beginning with the annual report for our fiscal year ending December 31, 2015. When we lose our status as an "emerging growth company" and reach an accelerated filer threshold, our independent registered public accounting firm will be required to attest to the effectiveness of our internal control

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over financial reporting. However, for so long as we remain an emerging growth company, we intend to take advantage of an exemption available to emerging growth companies from these auditor attestation requirements. The rules governing the standards that must be met for management to assess our internal control over financial reporting are complex and require significant documentation, testing, and possible remediation. To comply with the requirements of being a reporting company under the Exchange Act, we will need to upgrade our systems including information technology; implement additional financial and management controls, reporting systems, and procedures; and hire additional accounting and finance staff. If we or, if required, our auditors are unable to conclude that our internal control over financial reporting is effective, investors may lose confidence in our financial reporting, and the trading price of our common stock may decline.

We cannot assure you that there will not be material weaknesses or significant deficiencies in our internal control over financial reporting in the future. Any failure to maintain internal control over financial reporting could severely inhibit our ability to accurately report our financial condition, results of operations or cash flows. If we are unable to conclude that our internal control over financial reporting is effective, or if our independent registered public accounting firm determines we have a material weakness or significant deficiency in our internal control over financial reporting once that firm begins its Section 404 reviews, we could lose investor confidence in the accuracy and completeness of our financial reports, the market price of our common stock could decline, and we could be subject to sanctions or investigations by The NASDAQ Stock Market, the Securities and Exchange Commission (SEC) or other regulatory authorities. Failure to remedy any material weakness in our internal control over financial reporting, or to implement or maintain other effective control systems required of public companies, could also restrict our future access to the capital markets.

An active trading market for our common stock may not develop.

Prior to this offering, there has been no public market for our common stock. Although we have applied to list on common stock on The NASDAQ Global Market, an active trading market for our shares may never develop or be sustained following this offering. If the market does not develop or is not sustained, it may be difficult for you to sell your shares of common stock at a price that is attractive to you or at all. In addition, an inactive market may impair our ability to raise capital by selling shares and may impair our ability to acquire other companies or technologies by using our shares as consideration, which, in turn, could materially adversely affect our business.

The trading price of the shares of our common stock could be highly volatile, and purchasers of our common stock could incur substantial losses.

Our stock price is likely to be volatile. The stock market in general and the market for biotechnology companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, investors may not be able to sell their common stock at or above the initial public offering price. The market price for our common stock may be influenced by many factors, including:

- our ability to enroll subjects in our planned clinical trials;
- results of the clinical trials, and the results of trials of our competitors or those of other companies in our market sector;
- regulatory developments in the United States and foreign countries;
- variations in our financial results or those of companies that are perceived to be similar to us;
- changes in the structure of healthcare payment systems, especially in light of current reforms to the U.S. healthcare system;
- announcements by us or our competitors of significant acquisitions, strategic partnerships, joint ventures or capital commitments;
- market conditions in the pharmaceutical and biotechnology sectors and issuance of securities analysts' reports or recommendations;
- sales of our stock by insiders and stockholders;
- trading volume of our common stock;
- general economic, industry and market conditions other events or factors, many of which are beyond our control;
- additions or departures of key personnel; and
- intellectual property, product liability or other litigation against us.

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In addition, in the past, stockholders have initiated class action lawsuits against biotechnology and pharmaceutical companies following periods of volatility in the market prices of these companies' stock. Such litigation, if instituted against us, could cause us to incur substantial costs and divert management's attention and resources, which could have a material adverse effect on our business, financial condition and results of operations.

Our quarterly operating results may fluctuate significantly.

We expect our operating results to be subject to quarterly fluctuations. Our net loss and other operating results will be affected by numerous factors, including:

- variations in the level of expenses related to our clinical trial and development programs;
- addition or termination of clinical trials;
- any intellectual property infringement lawsuit in which we may become involved;
- regulatory developments affecting AVA-101 and our other product candidates;
- our execution of any collaborative, licensing or similar arrangements and the timing of payments we may make or receive under these arrangements;
- nature and terms of stock-based compensation grants; and
- derivative instruments recorded at fair value.

If our quarterly operating results fall below the expectations of investors or securities analysts, the price of our common stock could decline substantially. Furthermore, any quarterly fluctuations in our operating results may, in turn, cause the price of our stock to fluctuate substantially.

Our failure to meet the continued listing requirements of The NASDAQ Global Market could result in a delisting of our common stock.

If, after listing, we fail to satisfy the continued listing requirements of The NASDAQ Global Market, such as the corporate governance requirements or the minimum closing bid price requirement, NASDAQ may take steps to de-list our common stock. Such a delisting would likely have a negative effect on the price of our common stock and would impair your ability to sell or purchase our common stock when you wish to do so. In the event of a delisting, we would expect to take actions to restore our compliance with NASDAQ's listing requirements, but we can provide no assurance that any such action taken by us would allow our common stock to become listed again, stabilize the market price or improve the liquidity of our common stock, prevent our common stock from dropping below the NASDAQ minimum bid price requirement or prevent future non-compliance with NASDAQ's listing requirements.

We may allocate the net proceeds from this offering in ways that you and other stockholders may not approve.

Our management will have broad discretion in the application of the net proceeds from this offering, including for any of the purposes described in the section entitled "Use of Proceeds," and you will not have the opportunity as part of your investment decision to assess whether the net proceeds are being used appropriately. Because of the number and variability of factors that will determine our use of the net proceeds from this offering, their ultimate use may vary substantially from their currently intended use. Our management might not apply our net proceeds in ways that ultimately increase the value of your investment. We currently intend to use the net proceeds received by us from this offering as set forth under the caption "Use of Proceeds" on page 49 of this prospectus. The failure by our management to apply these funds effectively could harm our business. Pending their use, we may invest the net proceeds from this offering in short- and intermediate-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. These investments may not yield a favorable return to our stockholders. If we do not invest or apply the net proceeds from this offering in ways that enhance stockholder value, we may fail to achieve expected financial results, which could cause our stock price to decline.

You will suffer immediate and substantial dilution in the net tangible book value of the common stock you purchase.

The initial public offering price of our common stock is substantially higher than the pro forma as adjusted net tangible book value per share of our outstanding common stock immediately after the completion of this offering. Purchasers of common stock in this offering will experience immediate dilution of approximately \$9.74 per share, assuming an initial public offering price of \$16.50 per share, the midpoint of the range set forth on the cover of this prospectus, and the sale of stock in the concurrent private placement. In the past, we issued options and warrants to acquire common stock at prices significantly below the initial public offering price. To the extent these outstanding

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options and warrants are ultimately exercised, investors purchasing common stock in this offering will sustain further dilution. For a further description of the dilution that you will experience immediately after this offering, see "Dilution."

Because a small number of our existing stockholders own a majority of our voting stock, your ability to influence corporate matters will be limited.

Following the completion of this offering and the concurrent private placement, our executive officers, directors and greater than 5% stockholders, in the aggregate, will own approximately 59% of our outstanding common stock. As a result, such persons, acting together, will have the ability to control our management and affairs and substantially all matters submitted to our stockholders for approval, including the election and removal of directors and approval of any significant transaction. These persons will also have the ability to control our management and business affairs. This concentration of ownership may have the effect of delaying, deferring or preventing a change in control, impeding a merger, consolidation, takeover or other business combination involving us, or discouraging a potential acquirer from making a tender offer or otherwise attempting to obtain control of our business, even if such a transaction would benefit other stockholders.

Anti-takeover provisions in our charter documents and under Delaware law could make an acquisition of us, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current management.

Provisions in our amended and restated certificate of incorporation and amended and restated bylaws that will be in effect upon completion of this offering may delay or prevent an acquisition of us or a change in our management. These provisions include:

- authorizing the issuance of "blank check" preferred stock, the terms of which may be established and shares of which may be issued without stockholder approval;
- limiting the removal of directors by the stockholders;
- creating a staggered board of directors;
- prohibiting stockholder action by written consent, thereby requiring all stockholder actions to be taken at a meeting of our stockholders;
- eliminating the ability of stockholders to call a special meeting of stockholders;
- permitting our board of directors to accelerate the vesting of outstanding option grants upon certain transactions that result in a change of control; and
- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted upon at stockholder meetings.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which limits the ability of stockholders owning in excess of 15% of our outstanding voting stock to merge or combine with us. Although we believe these provisions collectively provide for an opportunity to obtain greater value for stockholders by requiring potential acquirors to negotiate with our board of directors, they would apply even if an offer rejected by our board were considered beneficial by some stockholders. In addition, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors, which is responsible for appointing the members of our management.

We do not intend to pay dividends on our common stock, and, consequently, your ability to achieve a return on your investment will depend on appreciation, if any, in the price of our common stock.

We have never declared or paid any cash dividend on our common stock and do not currently intend to do so for the foreseeable future. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future. Any return to stockholders will therefore be limited to the appreciation of their stock. Therefore, the success of an investment in shares of our common stock will depend upon any future appreciation in their value. There is no guarantee that shares of our common stock will appreciate in value or even maintain the price at which our stockholders have purchased their shares.

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Sales of a substantial number of shares of our common stock in the public market or the perception that these sales might occur, could significantly reduce the market price of our common stock and impair our ability to raise adequate capital through the sale of additional equity securities.

Based on shares of common stock outstanding as of March 31, 2014, upon the closing of this offering and the concurrent private placement, we will have outstanding a total of 20,775,103 shares of common stock giving effect to this offering, the concurrent private placement and the Transactions, assuming no exercise of the underwriters' option to purchase additional shares and no exercise of outstanding options. Of these shares, only the 5,400,000 shares of common stock sold in this offering by us, plus any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable without restriction in the public market immediately following this offering, unless they are purchased by one of our affiliates.

Our directors and executive officers and holders of substantially all of our outstanding securities have entered into lock-up agreements with the underwriters pursuant to which they may not, with limited exceptions, for a period of 180 days from the date of this prospectus, offer, sell or otherwise transfer or dispose of any of our securities, without the prior written consent of Jefferies LLC and Cowen and Company, LLC. The underwriters may, however, in their sole discretion, permit our officers, directors and other stockholders and the holders of our outstanding options and warrants who are subject to the lock-up agreements to sell shares prior to the expiration of the lock-up agreements. See "Underwriting—No Sales of Similar Securities." Sales of these shares, or perceptions that they will be sold, could cause the trading price of our common stock to decline.

After the lock-up agreements expire, up to an additional 15,301,727 shares of common stock will be eligible for sale in the public market of which 11,106,364 shares are held by directors, executive officers and other affiliates and will be subject to Rule 144 under the Securities Act. In addition, 7,025,565 shares of common stock that are either subject to outstanding options or reserved for future issuance under our employee benefit plans will become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules, the lock-up agreements and Rule 144 and Rule 701 under the Securities Act. If these additional shares of common stock are sold, or if it is perceived that they will be sold, in the public market, the trading price of our common stock could decline.

After this offering, the holders of 11,883,268 shares of our outstanding common stock, or approximately 57% of our total outstanding common stock, will be entitled to rights with respect to the registration of their shares under the Securities Act, subject to the 180-day lock-up agreements described above. See "Description of Capital Stock—Registration Rights." Registration of these shares under the Securities Act would result in the shares becoming freely tradable without restriction under the Securities Act, except for shares held by affiliates, as defined in Rule 144 under the Securities Act. Any sales of securities by these stockholders could have a material adverse effect on the trading price of our common stock.

We are an emerging growth company, and the reduced reporting requirements applicable to emerging growth companies may make our common stock less attractive to investors.

We are an emerging growth company, as defined in the JOBS Act. For as long as we continue to be an emerging growth company, we may take advantage of exemptions from various reporting requirements that are applicable to other public companies that are not emerging growth companies, including not being required to comply with the auditor attestation requirements of Section 404 of Sarbanes-Oxley, reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements and exemptions from the requirements of holding nonbinding advisory votes on executive compensation and stockholder approval of any golden parachute payments not previously approved. We could be an emerging growth company until the last day of the fiscal year following the fifth anniversary of this offering, although circumstances could cause us to lose that status earlier, including if we become a large accelerated filer (in which case we will cease to be an emerging company as of the date we become a large accelerated filer, which, generally, would occur if, at the end of a fiscal year, among other things, the market value of our common stock that is held by non-affiliates exceeds \$700 million as of the last business day of our most recently completed second fiscal quarter), if we have total annual gross

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revenue of \$1.0 billion or more during any fiscal year (in which cases we would no longer be an emerging growth company as of December 31 of such fiscal year), or if we issue more than \$1.0 billion in non-convertible debt during any three year period before that time (in which case we would cease to be an emerging growth company immediately). Even after we no longer qualify as an emerging growth company, we may still qualify as a "smaller reporting company," which would allow us to take advantage of many of the same exemptions from disclosure requirements including not being required to comply with the auditor attestation requirements of Section 404 of Sarbanes-Oxley and reduced disclosure obligations regarding executive compensation in this prospectus and our periodic reports and proxy statements. We cannot predict if investors will find our common stock less attractive because we may rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

We will incur significant increased costs as a result of operating as a public company, and our management will be required to devote substantial time to new compliance initiatives.

As a public company, we will incur significant legal, accounting and other expenses that we did not incur as a private company. We will be subject to the reporting requirements of the Exchange Act, which will require, among other things, that we file with the SEC annual, quarterly and current reports with respect to our business and financial condition. In addition, Sarbanes-Oxley, as well as rules subsequently adopted by the SEC, and The NASDAQ Global Market to implement provisions of Sarbanes-Oxley, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. Further, pursuant to the Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, the SEC to adopt additional rules and regulations in these areas, such as mandatory "say on pay" voting requirements that will apply to us when we cease to be an emerging growth company. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which may lead to additional compliance costs and impact the manner in which we operate our business in ways we cannot currently anticipate.

We expect the rules and regulations applicable to public companies to substantially increase our legal and financial compliance costs and to make some activities more time-consuming and costly. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will decrease our net income or increase our net loss, and may require us to reduce costs in other areas of our business or increase the prices of our products or services. For example, we expect these rules and regulations to make it more difficult and more expensive for us to obtain director and officer liability insurance, and we may be required to incur substantial costs to maintain the same or similar coverage. We cannot predict or estimate the amount or timing of additional costs we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers.

If securities or industry analysts do not publish research or reports or publish unfavorable research or reports about our business, our stock price and trading volume could decline.

The trading market for our common stock will depend in part on the research and reports that securities or industry analysts publish about us, our business, our market or our competitors. We do not currently have and may never obtain research coverage by securities and industry analysts. If no securities or industry analysts commence coverage of our company, the trading price for our stock would be negatively impacted. In the event we obtain securities or industry analyst coverage, if one or more of the analysts who covers us downgrades our stock, our stock price would likely decline. If one or more of these analysts ceases to cover us or fails to regularly publish reports on us, interest in our stock could decrease, which could cause our stock price or trading volume to decline.

Our ability to use net operating loss carryforwards and other tax attributes may be limited by the Internal Revenue Code.

We have incurred substantial losses during our history and do not expect to become profitable in the near future and we may never achieve profitability. To the extent that we continue to generate taxable losses, unused losses will carry forward to offset future taxable income, if any, until such unused losses expire. At December 31, 2013, we had federal and state net operating loss carryforwards of approximately \$4.5 million and \$5.4 million, respectively, which, if not utilized, begin to expire in various amounts beginning in the year 2026. If over a rolling three-year period, the cumulative change in our ownership exceeds 50 percentage points (as determined under applicable

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Treasury regulations) under Section 382 of the Internal Revenue Code of 1986, as amended (Code), our ability to utilize our U.S. federal net operating loss (NOL) carryforwards and other pre-change tax attributes (such as research tax credits) to offset future taxable income or taxes may be limited. We have experienced at least two ownership changes since inception and our utilization of NOL carryforwards will therefore be subject to annual limitation. Our ability to utilize our NOL carryforwards may be further limited as a result of subsequent ownership changes, including potential changes in connection with our proposed initial public offering. Similar rules may apply under state tax laws. We have not yet determined the amount of the cumulative change in our ownership resulting from this offering or any resulting tax loss limitations. Such limitations could result in the expiration of our carryforwards before they can be utilized and, if we are profitable, our future cash flows could be adversely affected due to our increased tax liability.

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This prospectus contains forward-looking statements that involve risks and uncertainties. All statements other than statements of historical facts contained in this prospectus are forward-looking statements. In some cases, you can identify forward-looking statements by terminology such as “may,” “could,” “will,” “would,” “should,” “expect,” “plan,” “anticipate,” “believe,” “estimate,” “intend,” “predict,” “seek,” “contemplate,” “potential” or “continue” or the negative of these terms or other comparable terminology. These forward-looking statements include, but are not limited to, statements about:

- the anticipated timing, costs and conduct of our planned clinical trials for our AVA-101, AVA-201, AVA 311 and other product candidates in our development program;
- our ability to advance our viral vector manufacturing and delivery capabilities;
- the timing or likelihood of regulatory filings and approvals;
- our plans to explore potential applications of our Ocular BioFactory platform in other indications in ophthalmology;
- our expectations regarding the clinical effectiveness of our product candidates;
- our commercialization, marketing and manufacturing capabilities and strategy;
- the pricing and reimbursement of our product candidates, if approved;
- our intellectual property position;
- the potential benefits of strategic collaborations and our ability to enter into strategic arrangements;
- our expectations related to the use of proceeds from this offering; and
- our estimates regarding expenses, future revenue, capital requirements and needs for additional financing.

These statements relate to future events or to our future financial performance and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. Factors that may cause actual results to differ materially from current expectations include, among other things, those listed under “Risk Factors” and elsewhere in this prospectus.

Any forward-looking statement in this prospectus reflects our current views with respect to future events and is subject to these and other risks, uncertainties and assumptions relating to our operations, results of operations, industry and future growth. Given these uncertainties, you should not place undue reliance on these forward-looking statements. These forward looking statements speak only as of the date of this prospectus. Except as required by law, we assume no obligation to update or revise these forward-looking statements for any reason, even if new information becomes available in the future.

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MARKET, INDUSTRY AND OTHER DATA

This prospectus contains estimates, projections and other information concerning our industry, our business and the markets for certain drugs, including data regarding the estimated size of those markets, their projected growth rates and the incidence of certain medical conditions. Information that is based on estimates, forecasts, projections or similar methodologies is inherently subject to uncertainties and actual events or circumstances may differ materially from events and circumstances reflected in this information. Unless otherwise expressly stated, we obtained this industry, business, market and other data from reports, research surveys, studies and similar data prepared by third parties, industry, medical and general publications, government data and similar sources. In some cases, we do not expressly refer to the sources from which this data is derived. In that regard, when we refer to one or more sources of this type of data in any paragraph, you should assume that other data of this type appearing in the same paragraph is derived from the same sources, unless otherwise expressly stated or the context otherwise requires.

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We estimate that the net proceeds from this offering will be approximately \$80.6 million at an assumed initial public offering price of \$16.50 per share, the midpoint of the estimated range shown on the cover page of this prospectus, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. If the underwriters exercise in full their option to purchase additional shares of common stock, we estimate that the net proceeds will be approximately \$93.0 million after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. In addition, upon the closing of this offering, we will receive gross proceeds from the sale of approximately \$10.0 million of shares of our common stock which Regeneron has contractually agreed to purchase in the concurrent private placement at the public offering price. Each \$1.00 increase or decrease in the assumed initial public offering price of \$16.50 would increase or decrease, respectively, our net proceeds by approximately \$5.0 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase or decrease of 1,000,000 in the number of shares we are offering would increase or decrease, respectively, the net proceeds to us from this offering, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, by approximately \$15.3 million, assuming the assumed initial public offering price stays the same.

We currently expect to use our net proceeds from this offering and the concurrent private placement as follows:

- approximately \$20 million to fund Phase 3 research and development start up activities for our AVA-101 study to evaluate safety and efficacy in subjects with wet AMD;
- approximately \$15 million to fund direct Phase 1/2 research and development expenses for our AVA-201 product candidates and other potential product candidates in our development program; and
- the remainder for potential future research and development programs, including our share of development costs for additional therapeutic targets we may choose to pursue under our collaboration with Regeneron, as well as capital expenditures, working capital and other general corporate purposes.

However, due to the uncertainties inherent in the product development and commercialization process, it is difficult to estimate with certainty the exact amounts of the net proceeds from this offering and the concurrent private placement that may be used for the above purposes. Our management will have sole and broad discretion over the use of the net proceeds from this offering and the concurrent private placement. The amounts and timing of our expenditures will depend upon numerous factors including the results of our research and development efforts, the timing and success of preclinical studies and any ongoing clinical trials or clinical trials we may commence in the future, the timing of regulatory submissions, the amount of cash, if any, generated by our collaboration with Regeneron and any future collaboration partners and any unforeseen cash needs.

We do not anticipate that net proceeds from this offering and the concurrent private placement will enable us to complete our Phase 3 trials or our Phase 1/2 trials of AVA-101 or our other product candidates and we will require substantial future capital in order to complete the remaining clinical development and to potentially commercialize these product candidates. See "Risk Factors—Risks Related to Our Financial Position and Need for Capital—If we fail to obtain the capital necessary to fund our operations, we will be unable to successfully develop and commercialize AVA-101 and our other product candidates."

Pending the use of the proceeds as described above, we intend to invest the net proceeds in interest-bearing investment-grade securities or government securities.

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DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We intend to retain all available funds and any future earnings, if any, to fund the development and expansion of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination related to dividend policy will be made at the discretion of our board of directors.

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CAPITALIZATION

The following table sets forth our cash and capitalization as of March 31, 2014:

- on an actual basis;
- on a subsequent events pro forma basis to give effect to the following transactions that occurred in April 2014 that affected our cash and capitalization, as if they had occurred as of March 31, 2014: (1) the issuance of 7,025,888 shares of Series B convertible preferred stock in April 2014 in exchange for \$52.9 million in cash; (2) the conversion of \$2.0 million of principal amount of outstanding convertible notes into 295,115 shares of Series B convertible preferred stock and the related loss on extinguishment of related-party convertible notes of \$0.2 million and repurchase of beneficial conversion feature of \$2.0 million; and (3) the repurchase of 531,208 shares of Series A convertible preferred stock in April 2014 for \$4.0 million in cash;
- on a pro forma basis to give further effect to the Transactions immediately prior to the completion of this offering; and
- on a pro forma as adjusted basis to give further effect to (1) the sale of 5,400,000 shares of common stock in this offering at an assumed initial public offering price of \$16.50 per share, the midpoint of the estimated price range set forth on the cover page of this prospectus, after deducting the underwriting discount and commissions, and estimated offering expenses payable by us, and (2) the sale of approximately \$10.0 million of shares of common stock in the concurrent private placement to Regeneron (or 606,060 shares at the assumed public offering price of \$16.50 per share).

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You should read this information together with our consolidated financial statements and related notes appearing elsewhere in this prospectus and the information set forth under the headings "Selected Consolidated Financial Data" and "Management's Discussion and Analysis of Financial Condition and Results of Operations."

	AS OF MARCH 31, 2014			
	ACTUAL	SUBSEQUENT EVENTS PRO FORMA	PRO FORMA	PRO FORMA AS ADJUSTED ⁽¹⁾
(In thousands, except share and per share data)				
Cash	\$ 169	\$ 50,074	\$ 50,679	\$ 141,242
Convertible preferred stock warrant liability	\$ 129	\$ 129	\$ —	\$ —
Series A convertible preferred stock, par value \$0.0001 per share: 4,233,295 shares authorized, 3,899,232 shares issued and outstanding, actual; 3,953,948 shares authorized, 3,368,024 shares issued and outstanding, subsequent events pro forma; no shares authorized pro forma and pro forma as adjusted, no shares issued and outstanding, pro forma and pro forma as adjusted	\$ 7,992	\$ 7,222	\$ —	\$ —
Series B convertible preferred stock, par value \$0.0001 per share: no shares authorized, no shares issued and outstanding, actual; 7,434,000 shares authorized and 7,321,003 shares issued and outstanding, subsequent events pro forma; no shares authorized pro forma and pro forma as adjusted, no shares issued and outstanding, pro forma and pro forma as adjusted	—	55,127	—	—
Stockholders' deficit:				
Preferred stock, par value \$0.0001 per share: no shares authorized, issued and outstanding, actual; 5,000,000 shares authorized, pro forma and pro forma as adjusted, no shares issued and outstanding, pro forma and pro forma as adjusted	—	—	—	—
Common stock, \$0.0001 par value per share: 15,000,000 shares authorized, 3,672,885 shares issued and outstanding, actual; 23,578,000 shares authorized, 3,672,885 shares issued and outstanding, subsequent events pro forma; 300,000,000 shares authorized, pro forma and pro forma as adjusted, 14,769,043 shares issued and outstanding, pro forma, and 20,775,103 pro forma as adjusted	—	—	1	2
Additional paid-in capital	1,788	—	63,082	153,644
Accumulated other comprehensive income	27	27	27	27
Deficit accumulated during the development stage	(10,532)	(13,196)	(13,196)	(13,196)
Total stockholders' equity (deficit)	(8,717)	(13,169)	49,914	140,477
Total capitalization	\$ (725)	\$ 49,180	\$ 49,914	\$ 140,477

⁽¹⁾ Each \$1.00 increase or decrease in the assumed initial public offering price of \$16.50 per share would increase or decrease, respectively, the amount of cash, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by approximately \$5.0 million, assuming the number of shares offered by us, as set forth on the cover page of this prospectus, and in the concurrent private placement, remains the same, and after deducting the underwriting discounts and commissions and estimated offering expenses payable by us. We may also increase or decrease the number of shares we are offering. An increase or decrease of 1,000,000 in the number of shares we are offering would increase or decrease, respectively, the amount of cash, additional paid-in capital, total stockholders' equity (deficit) and total capitalization by approximately \$15.3 million, assuming (i) the assumed initial public offering price per share, as set forth on the cover page of this prospectus, remains the same and (ii) the number of shares we issue and sell to Regeneron in the concurrent private placement remains the same. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

The number of shares of common stock issued and outstanding actual, subsequent events pro forma, pro forma and pro forma as adjusted in the table above excludes the following shares as of March 31, 2014:

- 4,134,200 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2014 under our Amended and Restated 2006 Equity Incentive Plan, at a weighted-average exercise price of \$0.47 per share;

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- 105,800 shares of common stock reserved for issuance pursuant to future awards under our Amended and Restated 2006 Equity Incentive Plan as of March 31, 2014;
- 2,088,332 shares of common stock reserved for issuance pursuant to future awards under our 2014 Equity Incentive Award Plan (subject to automatic annual adjustment in accordance with the terms of the plan), which will become effective immediately prior to the effectiveness of the registration statement to which this prospectus relates, of which options to purchase 455,000 shares of common stock at an exercise price equal to the initial public offering price set forth on the cover of this prospectus will be granted coincident with this offering, of which 375,000 shares will be awarded to executive officers and non-employee directors; and
- 208,833 shares of common stock reserved for issuance pursuant to future awards under our 2014 Employee Stock Purchase Plan, which will become effective immediately prior to the effectiveness of the registration statement to which this prospectus relates.

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If you invest in our common stock in this offering, your ownership interest will be diluted to the extent of the difference between the assumed initial public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock immediately after this offering.

Net tangible book value per share is determined by dividing our total tangible assets less our total liabilities by the number of shares of common stock outstanding. Our historical net tangible book value as of March 31, 2014 was \$(725,000), or \$(0.20) per share. Our pro forma net tangible book value as of March 31, 2014 was \$49.8 million, or \$3.47 per share, based on the total number of shares of our common stock outstanding as of March 31, 2014, after giving effect to the Transactions, the issuance of 7,321,003 shares of Series B convertible preferred stock and the repurchase of 531,208 shares of Series A convertible preferred stock in April 2014 as if they had occurred as of March 31, 2014.

Net tangible book value dilution per share to new investors represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the pro forma as adjusted net tangible book value per share of common stock immediately after completion of this offering. After giving effect to our sale of 5,400,000 shares of common stock in this offering at an assumed initial public offering price of \$16.50 per share, the midpoint of the estimated range set forth on the cover page of this prospectus, after deducting underwriting discounts and commissions and estimated offering expenses payable by us, and the sale of 606,060 shares of common stock in the concurrent private placement to Regeneron at an assumed initial public offering price of \$16.50 per share, our pro forma as adjusted net tangible book value as of March 31, 2014 would have been \$140.5 million, or \$6.76 per share. This represents an immediate increase in net tangible book value of \$3.29 per share to existing stockholders and an immediate dilution in net tangible book value of \$9.74 per share to purchasers of common stock in this offering, as illustrated in the following table:

Assumed initial public offering price per share		\$16.50
Pro forma net tangible book value per share as of March 31, 2014	\$3.47	
Increase in pro forma net tangible book value per share attributable to new investors in this offering	<u>\$3.29</u>	
Pro forma as adjusted net tangible book value per share after this offering and the concurrent private placement		<u>\$ 6.76</u>
Dilution per share to investors participating in this offering		<u>\$ 9.74</u>

Each \$1.00 increase or decrease in the assumed public offering price of \$16.50 per share, the mid-point of the price range set forth on the cover page of this prospectus, would increase or decrease, respectively, our pro forma as adjusted net tangible book value by \$5.0 million, or \$0.24 per share, and the pro forma dilution per share to investors in this offering by \$0.76 per share, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting underwriting discounts and commissions, and estimated offering expenses payable by us. If the underwriters' option to purchase additional shares from us is exercised in full, the pro forma as adjusted net tangible book value per share after this offering would be \$7.08 per share, the increase in pro forma as adjusted net tangible book value per share to existing stockholders would be \$3.62 per share and the dilution to new investors purchasing shares in this offering would be \$9.42 per share. We may also increase or decrease the number of shares we are offering. Assuming the assumed public offering price per share remains the same, after deducting the underwriting discounts and commissions and estimated offering expenses payable by us, an increase of 1,000,000 in the number of shares we are offering would increase our pro forma as adjusted net tangible book value by approximately \$15.3 million, or \$0.39 per share, the increase in pro forma as adjusted net tangible book value per share to existing stockholders would be \$3.69 per share and the dilution to new investors purchasing shares in this offering would be \$9.34 per share. The pro forma as adjusted information is illustrative only, and we will adjust this information based on the actual initial public offering price and other terms of this offering determined at pricing.

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The following table presents, on a pro forma as adjusted basis as of March 31, 2014 after giving effect to the Transactions, the issuance of 7,321,003 shares Series B convertible preferred stock in April 2014, the repurchase of 531,208 shares of Series A convertible preferred stock in April 2014 and the concurrent private placement to Regeneron, and assuming that our existing stockholders do not purchase shares of our common stock in this offering, the differences between the existing stockholders and the purchasers of shares in this offering with respect to the number of shares purchased from us, the total consideration paid, which includes net proceeds received from the issuance of common and preferred stock, cash received from the exercise of stock options and warrants and the value of any stock issued for services and the average price paid per share (in thousands, except per share amounts and percentages):

	SHARES PURCHASED		TOTAL CONSIDERATION		AVERAGE PRICE PER SHARE
	NUMBER	PERCENT	AMOUNT	PERCENT	
Existing stockholders	14,769,043	71%	\$ 57,165,249	37%	\$ 3.87
New investors	6,006,060	29%	99,099,990	63%	\$ 16.50
Totals	<u>20,775,103</u>	<u>100%</u>	<u>156,265,239</u>	<u>100%</u>	\$ 7.52

The foregoing calculations exclude the following shares as of March 31, 2014:

- 4,134,200 shares of common stock issuable upon exercise of stock options outstanding as of March 31, 2014 under our Amended and Restated 2006 Equity Incentive Plan, at a weighted-average exercise price of \$0.47 per share;
- 105,800 shares of common stock reserved for issuance pursuant to future awards under our Amended and Restated 2006 Equity Incentive Plan as of March 31, 2014;
- 2,088,332 shares of common stock reserved for issuance pursuant to future awards under our 2014 Equity Incentive Award Plan (subject to automatic annual adjustment in accordance with the terms of the plan), which will become effective immediately prior to the effectiveness of the registration statement to which this prospectus relates, of which options to purchase 455,000 shares of common stock at an exercise price equal to the initial public offering price set forth on the cover of this prospectus will be granted coincident with this offering, of which 375,000 shares will be awarded to executive officers and non-employee directors;
- 208,833 shares of common stock reserved for issuance pursuant to future awards under our 2014 Employee Stock Purchase Plan, which will become effective immediately prior to the effectiveness of the registration statement to which this prospectus relates;

If the underwriters exercise in full their option to purchase additional shares of our common stock, our existing stockholders would own 68% and our new investors would own 32% of the total number of shares of our common stock outstanding upon completion of this offering. The total consideration paid by our existing stockholders would be approximately \$57.2 million, or 34%, and the total consideration paid by our new investors would be \$112.5 million, or 66%.

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SELECTED CONSOLIDATED FINANCIAL DATA

The following selected consolidated financial data for the years ended December 31, 2012 and 2013 are derived from our audited consolidated financial statements appearing elsewhere in this prospectus. The selected financial data for the three months ended March 31, 2013 and 2014, and for the period from July 17, 2006 (date of inception) to March 31, 2014 and as of March 31, 2014 are derived from our unaudited consolidated financial statements appearing elsewhere in this prospectus. The unaudited consolidated financial statements have been prepared on the same basis as the audited consolidated financial statements and, in the opinion of management, reflect all adjustments, which include only normal recurring adjustments, necessary to present fairly our financial position as of March 31, 2014 and the results of operations for the three months ended March 31, 2013 and 2014, and for the period from July 17, 2006 (date of inception) to March 31, 2014. You should read this selected financial data together with our consolidated financial statements and related notes appearing elsewhere in this prospectus and the information under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations." Our historical results are not necessarily indicative of our future results and interim results are not necessarily indicative of results to be expected for the full year.

(In thousands, except share and per share data)	YEARS ENDED DECEMBER 31,		THREE MONTHS ENDED MARCH 31,		PERIOD FROM JULY 17, 2006 (INCEPTION) TO MARCH 31,
	2012	2013	2013	2014	2014
CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS DATA:					
Revenue:					
License revenue	\$ —	\$ —	\$ —	\$ 30	\$ 30
Government grant revenue	30	480	300	—	510
Total revenue	30	480	300	30	540
Operating expenses:					
Research and development	1,310	2,151	201	910	5,546
General and administrative	536	1,783	141	726	3,631
Total operating expenses	1,846	3,934	342	1,636	9,177
Operating loss	(1,816)	(3,454)	(42)	(1,606)	(8,637)
Interest expense, net	(8)	(73)	(13)	(14)	(114)
Other income (expense), net	7	(96)	6	(43)	(134)
Change in fair value of embedded derivative	6	18	—	—	24
Loss on extinguishment of related-party convertible notes	—	(1,671)	—	—	(1,671)
Net loss	(1,811)	(5,276)	(49)	(1,663)	(10,532)
Foreign currency translation adjustment	8	19	—	—	27
Comprehensive loss	\$ (1,803)	\$ (5,257)	\$ (49)	\$ (1,663)	\$ (10,505)
Net loss per share attributable to common stockholders — basic and diluted	\$ (0.50)	\$ (1.44)	\$ (0.01)	\$ (0.45)	
Weighted-average common shares outstanding — basic and diluted	3,642,503	3,672,885	3,672,885	3,672,885	
Pro forma net loss per share attributable to common stockholders — basic and diluted		\$ (0.74)		\$ (0.11)	
Pro forma weighted average common shares outstanding — basic and diluted		6,889,774		14,741,705	

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The table below presents our consolidated balance sheet data as of December 31, 2012 and 2013 and March 31, 2014:

(In thousands)	AS OF DECEMBER 31,		AS OF
	2012	2013	MARCH 31, 2014
CONSOLIDATED BALANCE SHEET DATA:			
Cash	\$ 357	\$ 564	\$ 169
Total assets	386	1,085	1,103
Convertible preferred stock warrant liability	36	91	129
Convertible preferred stock	2,471	7,992	7,992
Deficit accumulated during the development stage	(3,593)	(8,869)	(10,532)
Total stockholders' deficit	(3,468)	(8,210)	(8,717)

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Table of Contents**MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS**

You should read the following discussion and analysis of our financial condition and results of operations together with the section of this prospectus entitled "Selected Consolidated Financial Data" and our consolidated financial statements and related notes included elsewhere in this prospectus. This discussion and other parts of this prospectus contain forward-looking statements that involve risk and uncertainties, such as statements of our plans, objectives, expectations and intentions. Our actual results could differ materially from those discussed in these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in the section of this prospectus entitled "Risk Factors."

Overview

We are a clinical-stage biotechnology company focused on discovering and developing novel gene therapies to transform the lives of patients with sight-threatening ophthalmic diseases. We have leveraged our next-generation gene therapy platform, Ocular BioFactory, to create a robust pipeline of product candidates. Our product candidates are designed to provide long-term efficacy or a functional cure for these diseases by inducing a sustained expression of a therapeutic protein with a one-time administration in the eye.

We are targeting a variety of prevalent and rare genetic ophthalmic diseases with significant unmet medical need. Our lead product candidate is AVA-101 for the treatment of wet age-related macular degeneration (AMD). We believe that this product candidate could transform the treatment paradigm and address the unmet need in the large wet AMD market.

We have generated human proof-of-concept data for AVA-101 in a Phase 1 trial with eight wet AMD subjects conducted at LEI in Australia. In that Phase 1 trial, AVA-101 was well tolerated with no drug-related adverse events. In addition, subjects treated with AVA-101 showed meaningful improvement in their visual acuity test scores (up to 15 letter improvement on an eye chart from baseline), and most subjects did not receive any rescue injections of standard-of-care therapy (required for subjects exhibiting disease progression) during the one-year trial period. We are currently conducting a Phase 2a trial for AVA-101 in wet AMD. Interim drug safety surveillance data received in June 2014 from this ongoing study suggests that AVA-101 continues to be well tolerated. We expect to receive top-line data from this ongoing Phase 2a trial in mid-2015. We own exclusive rights to develop and commercialize AVA-101 worldwide.

In addition to AVA-101, our Ocular BioFactory platform has generated other promising product candidates for the treatment of severe ophthalmic diseases, including AVA-201 and AVA-311. We are developing AVA-201 as a next-generation product candidate for the prevention of wet AMD. AVA-201 produces the same anti-vascular endothelial growth factor (VEGF) protein as AVA-101 using a proprietary, customized delivery mechanism, or vector, that can be administered earlier in the disease progression, before the onset of wet AMD. We own worldwide rights to AVA-201. AVA-311 is being developed in collaboration with our partner Regeneron for the treatment of X-linked retinoschisis (XLR), a rare genetic disease of the retina with no approved therapy. Based on preclinical studies to date, AVA-311 has shown to delay the progression of XLR and improve vision by effectively delivering functional copies of the RS1 gene in retinal cells of mice.

In order to accelerate the pace of generating and developing product candidates for our pipeline, we entered into a broad research collaboration and license agreement with Regeneron in May 2014. Under the terms of the agreement, we intend to jointly discover novel product candidates based on our Ocular BioFactory platform for up to eight therapeutic targets including AVA-311. We have received initial payments of \$8.0 million as well as ongoing support for research and development, and we are eligible to receive up to \$80.0 million in development and regulatory milestone payments for product candidates directed toward each therapeutic target, for a combined total of up to \$640 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, and low- to mid-single-digit royalties on worldwide net sales of collaboration product candidates. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits.

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Table of Contents**Financial Overview****Summary**

We have not generated positive cash flow or net income from operations since our inception and, at March 31, 2014, we had an accumulated deficit of \$10.5 million, primarily as a result of research and development and general and administrative expenses. We expect to incur substantial losses from operations in the foreseeable future as we continue our research and development efforts, advance AVA-101 and other product candidates through preclinical and clinical development, manufacture clinical study materials, seek regulatory approval and prepare for, and if approved, proceed to commercialization. We are at an early stage of development and may never be successful in developing or commercializing our product candidates.

See “Risk Factors—Risks Related to Our Financial Position and Need for Capital—We have incurred significant operating losses since inception, and we expect to incur significant losses for the foreseeable future. We may never become profitable or, if achieved, be able to sustain profitability.”

While we may in the future generate revenue from a variety of sources, including license fees, milestone and research and development payments in connection with strategic partnerships, and potentially revenue from approved product sales, we have not yet generated any revenue from approved therapeutic product candidates.

Through March 31, 2014, we have financed our operations through private placements of convertible notes and preferred stock with our investors, funding under our government grants and licensing revenue from an agreement related to the licensing of certain of our intellectual property. We entered into our first license revenue generating agreement during the first quarter of 2014. We have never been profitable and have incurred net losses in each year since commencement of our operations.

We have no manufacturing facilities, and all of our manufacturing activities are contracted out to a third party. Additionally, we currently utilize third-party clinical research organizations (CROs) to carry out our clinical development and we do not yet have a sales organization.

We expect to incur significant and increasing losses from operations for the foreseeable future, and we can provide no assurance that we will ever generate significant revenue or profits. In April 2014, we received gross proceeds of \$52.9 million from the sale of shares of Series B convertible preferred stock, of which \$4.0 million was used to repurchase outstanding shares of Series A convertible preferred stock from an existing investor. We also converted the outstanding balance under our related-party convertible notes of \$2.0 million into shares of Series B convertible preferred stock. In May 2014, we received initial payments of \$8.0 million in connection with our collaboration with Regeneron. With these amounts and our existing cash balances as of March 31, 2014, we believe we will have sufficient funds to operate through at least December 31, 2015.

We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of AVA-101 and any additional product candidates. Specifically, we have incurred and we expect to continue to incur substantial expenses in connection with our existing Phase 2a clinical trial and any Phase 2b and Phase 3 clinical trials that we may conduct for AVA-101. We will need substantial additional funding to support our operating activities as we advance AVA-101 and other potential product candidates through clinical development, seek regulatory approval and prepare for, and if approved, proceed to commercialization. Adequate funding may not be available to us on acceptable terms, or at all.

Revenue

To date, we have not generated any revenue from the sale of our products. As of March 31, 2014, we had only generated revenue from government grants and \$30,000 of license revenue pursuant to a license agreement related to the licensing of certain of our intellectual property. We have no future obligations under this agreement. Subsequent to March 31, 2014, we received initial payments of \$8.0 million pursuant to our research collaboration and license agreement with Regeneron.

Our ability to generate product revenue and become profitable depends upon our ability to successfully develop and commercialize our product candidates. Because of the numerous risks and uncertainties associated with product development, we are unable to predict the amount or timing of product revenue. Even if we are able to generate revenue from the sale of our products, we may be unable to continue our operations at planned levels and be forced to reduce our operations.

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Table of Contents**Research and Development Expenses**

Conducting a significant amount of research and development is central to our business model. Research and development expenses include certain payroll and personnel expenses, stock-based compensation expense, laboratory supplies, consulting costs, external contract research and development expenses, including expenses incurred under agreements with CROs, the cost of acquiring, developing and manufacturing clinical study materials, and overhead expenses, including rent, equipment depreciation, insurance and utilities.

Research and development costs are expensed as incurred. Advance payments for goods or services for future research and development activities are deferred and expensed as the goods are delivered or the related services are performed.

We estimate preclinical study and clinical trial expenses based on the services performed pursuant to contracts with research institutions and CROs that conduct and manage preclinical studies and clinical trials on our behalf. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. We estimate the amounts incurred through communications with third party service providers and our estimates of accrued expenses as of each balance sheet date are based on information available at the time. If the actual timing of the performance of services or the level of effort varies from the estimate, we will adjust the accrual accordingly.

As we pursue the clinical development of our lead product candidate, AVA-101, the amount of research and development expenses will continue to grow. Product candidates in later stages of clinical development have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of late-stage clinical trials. Accordingly, we plan to increase our research and development expenses for the foreseeable future as we seek to complete the development and commercialization of AVA-101. The successful development and commercialization of AVA-101 is highly uncertain and we cannot reasonably estimate the nature, timing, or costs of the efforts that will be necessary to complete the remainder of the development of AVA-101 at this time. Clinical development timelines, the probability of success and development and commercialization costs can differ materially from expectations.

We received refundable tax credits from the Australian tax authorities in connection with certain research costs incurred by our subsidiary conducting research in Australia. These refunds do not depend on our taxable income or tax position and therefore we do not account for them under an income tax accounting model. We recognize such refunds as government grants in the period when qualified expenses are incurred as a reduction of research expenses. We have recorded the reimbursement from the Australian tax authorities as a reduction of research and development expense in the consolidated statements of operations and comprehensive loss for the applicable period.

General and Administrative Expenses

General and administrative expenses consist principally of personnel-related costs, stock-based compensation, professional fees for legal, consulting, audit and tax services, rent and other general operating expenses not otherwise included in research and development expenses. We anticipate general and administrative expenses will increase in future periods as we invest in the infrastructure needed to support continued research and development activities and potential commercialization of our product candidates. We also anticipate increased expenses related to audit, legal and regulatory functions, as well as director and officer insurance premiums and investor relations costs associated with being a public reporting company.

Other Income (Expense), Net

Other income (expense), net is comprised mainly of changes in the fair value of common stock warrant liabilities and preferred stock warrant liabilities. For a description of our valuation methods, see “—Estimated fair value of obligation to issue a common stock warrant and convertible preferred stock warrant liabilities” under “Critical accounting policies, significant judgments and use of estimates.”

Critical Accounting Policies, Significant Judgments and Use of Estimates

This discussion and analysis of our financial condition and results of operations is based on our consolidated financial statements, which have been prepared in accordance with GAAP. The preparation of these consolidated

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financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the consolidated financial statements, as well as the reported expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Revenue Recognition

We have primarily generated revenue through a license arrangement and government grants related to our research and development programs.

Government grants provide funds for certain types of expenditures in connection with research and development activities over a contractually defined period. Revenue related to government grants is recognized in the period during which the related costs are incurred and the related services are rendered, provided that the applicable performance obligations under the government grants have been met. We intend to continue to evaluate pursuing additional government grant opportunities on a case-by-case basis.

Funds received under government grants are recorded as revenue if we are deemed to be the principal participant in the contract arrangements because the activities under the contracts are part of our development programs. If we are not the principal participant, the funds from government grants are recorded as a reduction to research and development expense. Funds received from government grants are not refundable and are recognized when the related qualified research and development expenses are incurred and when there is reasonable assurance that the funds will be received. Funds received in advance of the performance of the services are recorded as deferred revenue.

Accrued Research and Development Expense

We estimate our accrued research and development expenses as of each balance sheet date. This process involves reviewing contracts and purchase orders, reviewing the terms of our license agreements, communicating with our applicable personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. Expenses that are paid in advance of performance are deferred as a prepaid expense and expensed as the services are provided.

Examples of estimated accrued research and development expenses include fees to:

- contract manufacturers in connection with the production of clinical trial materials;
- CROs and other service providers in connection with clinical studies;
- investigative sites in connection with clinical studies;
- vendors in connection with preclinical development activities; and
- services providers for professional service fees such as consulting and related services.

Our understanding of the status and timing of services performed relative to the actual status and timing may vary and may result in our reporting changes in estimates in any particular period. To date, there have been no material differences from our estimates to the amount actually incurred. However, due to the nature of these estimates, we cannot assure you that we will not adjust our estimates in the future as we become aware of additional information about the status or conduct of our clinical studies or other research activities.

Stock-Based Compensation Expense

We recognize compensation costs related to stock-based awards granted to employees based on the estimated fair value of the awards on the date of grant, net of estimated forfeitures. We estimate the grant date fair value, and the resulting stock-based compensation expense, using the Black-Scholes valuation model. The grant date fair value of the stock-based awards is generally recognized on a straight-line basis over the requisite service period, which is

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generally the vesting period of the respective awards. Stock-based compensation expense related to awards to non-employees is recognized based on the then-current fair value at each measurement date over the associated service period of the award, which is generally the vesting term, using the accelerated attribution method. We have used the Black-Scholes valuation model to assist us in determining the fair value of stock-based awards. The Black-Scholes valuation model requires the use of subjective and highly complex assumptions which determine the fair value of stock-based awards.

Stock Options Granted to Employees

The fair value of each option issued to employees was estimated at the date of grant using the Black-Scholes valuation model with the following weighted-average assumptions:

	YEAR ENDED DECEMBER 31,		THREE MONTHS ENDED MARCH 31,	
	2012	2013	2013	2014 (Unaudited)
Expected volatility	82%	80%	—	78%
Expected term (in years)	6.0	6.0	—	6.0
Risk-free interest rate	0.9%	1.0%	—	1.8%
Expected dividend yield	0.0%	0.0%	—	0.0%

As of December 31, 2013, there was \$0.4 million of unrecognized stock-based compensation expense related to employees' awards that is expected to be recognized over a weighted-average period of 2.9 years. As of March 31, 2014, there was \$1.2 million of unrecognized stock-based compensation expense related to employees' awards that is expected to be recognized over a weighted-average period of 2.8 years.

Stock Options Granted to Non-Employees

We used the following weighted-average assumptions in estimating non-employees stock-based compensation expense:

	YEAR ENDED DECEMBER 31,		THREE MONTHS ENDED MARCH 31,	
	2012	2013	2013	2014 (Unaudited)
Expected volatility	78%	79%	79%	77%
Expected term (in years)	9.0	7.9	8.2	7.8
Risk-free interest rate	1.6%	1.8%	1.6%	2.6%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

Expected volatility. Because we are a private entity with no historical data regarding the volatility of our common stock, the expected volatility used is based on volatility of a group of similar entities, referred to as "guideline" companies. In evaluating similarity, we considered factors such as industry, stage of life cycle and size. We will continue to apply this process until a sufficient amount of historical information regarding the volatility of our own stock price becomes available.

Expected term. We derived the expected term using the "simplified" method (the expected term is determined as the average of the time-to-vesting and the contractual life of the options), as we have limited historical information to develop expectations about future exercise patterns and post vesting employment termination behavior. Expected term for non-employee awards is based on the remaining contractual term of an option on each measurement date.

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Risk-free interest rate. The risk-free interest rate is based on U.S. Treasury zero-coupon issues with remaining terms similar to the expected term on the options.

Expected dividend yield. We have never paid any dividends and do not plan to pay dividends in the foreseeable future, and, therefore, used an expected dividend yield of zero in the valuation model.

Forfeitures. We estimate forfeitures at the time of grant, and revise those estimates in subsequent periods if actual forfeitures differ from those estimates. We use historical data to estimate pre-vesting option forfeitures and record stock-based compensation expense only for those awards that are expected to vest. To the extent actual forfeitures differ from the estimates, the difference will be recorded as a cumulative adjustment in the period that the estimates are revised.

The following table sets forth our total stock-based compensation expense for awards granted in the years ended December 31, 2012 and 2013 for the three months ended March 31, 2013 and 2014, and for the period from July 17, 2006 (date of inception) to December 31, 2013 and March 31, 2014 (in thousands):

	YEAR ENDED DECEMBER 31,		PERIOD FROM JULY 17, 2006 (DATE OF INCEPTION) TO DECEMBER 31,	THREE MONTHS ENDED MARCH 31,	PERIOD FROM JULY 17, 2006 (DATE OF INCEPTION) TO MARCH 31,
	2012	2013	2013	2013 2014	2014
				(Unaudited)	(Unaudited)
Research and development	\$ 54	\$ 362	\$ 441	\$ 33 \$69	\$ 510
General and administrative	22	153	175	35 46	221
Total	\$ 76	\$ 515	\$ 616	\$ 68 \$115	\$ 731

Fair value of common stock. The fair value of the shares of common stock underlying our stock options has historically been determined by our board of directors. Because there has been no public market for our common stock and in the absence of recent arm's-length cash sales transactions of our common stock with independent third parties, our board of directors has determined the fair value of our common stock by considering at the time of grant a number of objective and subjective factors, including the following: independent third-party valuations as of December 31, 2012, March 31, 2013, June 30, 2013, September 30, 2013, December 31, 2013 and March 31, 2014; progress of research and development activities; our operating and financial performance, including our levels of available capital resources; rights and preferences of our common stock compared to the rights and preferences of our other outstanding equity securities; equity market conditions affecting comparable public companies, as reflected in comparable companies' market multiples, initial public offering (IPO) valuations and other metrics; the achievement of enterprise milestones, including our progress in clinical trials and potential collaborations with partners; the likelihood of achieving a liquidity event for the shares of common stock, such as an IPO given prevailing market and biotechnology sector conditions; sales of our convertible preferred stock in arms-length transactions; the illiquidity of our securities by virtue of being a private company; business risks; and management and board experience.

The independent third-party valuations used the income, guideline and transaction approaches based on our expected future cash flows and applied a discount for lack of marketability. The guideline approach measures value on a minority-interest basis; the transaction and income approaches measure value on a controlling basis. This approach is outlined in the American Institute of Certified Public Accountants (AICPA) Practice Aid, "Valuation of Privately-Held-Company Equity Securities Issued as Compensation" as the probability-weighted expected return method (PWERM). Enterprise values were calculated based on three exit scenarios, including an IPO, a partnership for the development of our product candidate either in an earlier stage or a late stage of clinical development and a corporate failure. Each value was weighted based on the probability of each event's occurrence to arrive at an indicated enterprise value. In estimating the value of equities, management estimated a term for each of the IPO, partnership or corporate failure scenarios.

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Following the completion of this offering, the fair value of our common stock generally will be determined by reference to the closing sales price of a share of our common stock on the grant date.

Estimated Fair Value of Our Convertible Preferred Stock

In connection with the preparation of our consolidated financial statements for the year ended December 31, 2013 included in this prospectus, we prepared retrospective valuations of the fair value of our Series A convertible preferred stock for financial reporting purposes as of September 30, 2013, November 12, 2013 and December 31, 2013 to assist our board of directors in reevaluating the fair value of our convertible preferred stock. The estimated fair value of our Series A convertible preferred stock was determined using a PWERM model, as discussed above in the fair value of common stock. On August 28, 2012, we entered into a convertible note payable agreement with a related party investor for the issuance and sale of up to an aggregate principal amount of \$2.0 million of convertible notes (2012 Notes). On November 12, 2013, we issued 1,419,959 shares of Series A convertible preferred stock upon the conversion of the 2012 Notes, and issued 689,655 shares of Series A convertible preferred stock to a potential collaborator for cash, in each case at a price of \$1.45 per share. The estimated fair value of Series A convertible preferred stock was \$2.63 per share on the issuance date. In fiscal 2013, we recorded a loss on extinguishment of the 2012 Notes of \$1.7 million, and an expense of \$0.8 million associated with collaboration acquisitions costs which are recorded in general and administrative expense in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2013.

Estimated Fair Value of Obligation to Issue a Common Stock Warrant and Convertible Preferred Stock Warrant Liabilities

We previously issued warrants to purchase shares of our convertible preferred stock to certain investors in connection with convertible note purchase agreements entered into between 2006 and 2009. In addition, as of December 31, 2013, we had an obligation to issue a warrant to purchase common stock in connection with the license agreement we entered into with LEI in 2010. Both the convertible preferred stock warrants and the obligation to issue a warrant to purchase common stock are accounted for as liabilities and are initially recorded at fair value. We have recorded the obligation to issue a warrant to purchase common stock as a derivative liability as the terms of the warrants are not fixed due to potential adjustments in the exercise price issuable under the warrants. At each balance sheet date, gains and losses arising from changes in fair value of these liabilities are recognized in other income (expense), net in the consolidated statements of operations and comprehensive loss while such instruments are outstanding and classified as liabilities. The fair value of the liabilities is determined using an option pricing model, based on inputs as of the valuation measurement dates, including the estimated fair value of our stock, the estimated volatility of the price of our stock, the expected term of the warrants and the risk-free interest rates. Refer to Note 10, Warrants, for key assumptions used in the valuation at each reporting period, in our consolidated financial statements included elsewhere in this prospectus. The convertible preferred stock and common stock warrant liabilities will increase or decrease each period based on the fluctuations of the fair value of the underlying security. A significant fluctuation in the common or convertible preferred stock fair value would result in a material change in the fair values of the convertible preferred stock and common stock warrant liabilities.

We adjusted the obligation to issue a warrant to purchase common stock liability for changes in fair value on an ongoing basis until the warrant was issued in March 2014 and the exercise price for the warrants became fixed. At such time we reclassified the liability to additional paid-in capital and no further change in fair value will be recorded. However, we will continue to adjust the convertible preferred stock warrant liabilities for changes in fair value until the earlier of the expiration of the warrants, exercise of the warrants or conversion of the preferred stock underlying the warrants into common stock upon the completion of a liquidity event, including this offering, at which time the liabilities will be reclassified to additional paid-in capital.

Derivative Instruments

In connection with the 2012 Notes, we recorded an embedded derivative liability for the potential payments that would be made to holders of our 2012 Notes in the event of a change of control of our company prior to the maturity date of such notes. The embedded derivative liability is initially recorded at fair value, with gains and losses arising from changes in fair value recognized in other income (expense), net in the consolidated statements of operations and comprehensive loss at each period end while such notes are outstanding. The embedded derivative liability is being valued using a probability-weighted expected return model. We estimated a change of control event probability as 5%

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and used a discount rate of 21% when estimating fair value of embedded derivative during 2012 and 2013. The embedded derivative terminated when the 2012 Notes were converted into shares of Series A convertible preferred stock in November 2013.

Income Tax

We recognize deferred income taxes for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. We periodically evaluate the positive and negative evidence bearing upon realizability of our deferred tax assets. Based upon the weight of available evidence, which includes our historical operating performance, reported cumulative net losses since inception and difficulty in accurately forecasting our future results, we maintained a full valuation allowance on the net deferred tax assets as of December 31, 2012 and 2013 of approximately \$1.1 million and \$2.5 million, respectively. We intend to maintain a full valuation allowance on the federal, state and foreign deferred tax assets until sufficient positive evidence exists to support reversal of the valuation allowance.

As of December 31, 2013, we had NOL carryforwards of approximately \$4.5 million to offset future federal income, \$5.4 million that may offset future state income and \$70,000 that may offset future foreign income. If not utilized, the federal and state NOL carryforwards will begin to expire in various years beginning in 2026. The foreign NOL carryforwards do not expire.

Under Section 382 of the Code, our ability to utilize NOL carryforwards or other tax attributes such as research tax credits, in any taxable year may be limited if we have experienced an "ownership change." Generally, a Section 382 ownership change occurs if there is a cumulative increase of more than 50 percentage points in the stock ownership of one or more stockholders or groups of stockholders who own at least 5% of a corporation's stock within a specified testing period. Similar rules may apply under state tax laws. We believe that we have experienced at least two ownership changes under Section 382 which will result in limitations in our ability to utilize net operating losses and credits. In addition, we may experience ownership changes as a result of our proposed initial public offering, future offerings or other changes in the ownership of our stock. As a result, the amount of the NOL carryforwards and research and credit carryforwards presented in our financial statements could be limited and may expire unutilized.

We record unrecognized tax benefits as liabilities and adjust these liabilities when our judgment changes as a result of the evaluation of new information not previously available. Because of the complexity of some of these uncertainties, the ultimate resolution may result in a payment that is materially different from our current estimate of the unrecognized tax benefit liabilities. These differences will be reflected as increases or decreases to income tax expense in the period in which new information is available. Our policy is to recognize interest and penalties related to income taxes as a component of income tax expense. No interest and penalties related to income taxes have been recognized in the statements of operations and comprehensive loss in 2012 and 2013.

Emerging Growth Company Status

Section 107 of the JOBS Act provides that an emerging growth company can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act for complying with new or revised accounting standards. Thus, an emerging growth company can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have irrevocably elected not to avail ourselves of this extended transition period and, as a result, we will adopt new or revised accounting standards on the relevant dates on which adoption of such standards is required for companies that are not emerging growth companies.

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[Table of Contents](#)**Results of Operations****Comparison of the Three Months Ended March 31, 2013 and 2014**

The following table summarizes our results of operations for the periods indicated:

(in thousands)	THREE MONTHS ENDED MARCH 31,		INCREASE/ (DECREASE)
	2013	2014 (Unaudited)	
License revenue	\$ —	\$ 30	\$ 30
Government grant revenue	300	—	(300)
Total revenue	300	30	(270)
Operating expenses:			
Research and development	201	910	709
General and administrative	141	726	585
Total operating expenses	342	1,636	1,294
Operating loss	(42)	(1,606)	(1,564)
Interest expense	(13)	(14)	(1)
Other income (expense), net	6	(43)	(49)
Net loss	<u>\$ (49)</u>	<u>\$ (1,663)</u>	<u>\$ (1,614)</u>

Revenue

License revenue increased by \$30,000 during the three months ended March 31, 2014 as we earned revenue from a license agreement signed with a new partner during the period. Government grant revenue decreased from \$300,000 in the three months ended March 31, 2013 to zero in the three months ended March 31, 2014 as we completed the work performed under the grants during 2013. In May 2014, we received an upfront payment of \$8.0 million from Regeneron, which we expect to recognize as revenue during future periods.

Research and Development Expense

Research and development expense increased from \$0.2 million for the three months ended March 31, 2013 to \$0.9 million for the three months ended March 31, 2014. The increase in research and development expense was primarily due to an increase in payroll expenses of \$0.3 million for the first quarter of 2014 as a result of an increase in our employee headcount. Expenses during the three months ended March 31, 2013 benefitted from reimbursement of \$0.5 million from the Australian tax authorities recorded as a reduction in research and development expense as compared to \$46,000 during the comparable period in 2014. For the periods presented, substantially all of our research and development expense related to our development activity for AVA-101 for the treatment of wet AMD. We expect research and development expenses to increase in future periods as we continue the development of AVA-101 in late-stage clinical trials.

General and Administrative Expense

General and administrative expense increased from \$0.1 million for the three months ended March 31, 2013 to \$0.7 million for the three months ended March 31, 2014. The increase in general and administrative expense was primarily due to increases in payroll of \$0.2 million and consulting and professional service expenses of \$0.4 million as we expanded our operations. We expect general and administrative costs to increase in future periods, reflecting both the increased costs in connection with the future commercialization of AVA-101, as well as an expanded infrastructure and increased professional fees associated with being a public company.

Interest Expense

Interest expense increased from \$13,000 for the three months ended March 31, 2013 to \$14,000 for the comparable period in 2014. The increase was due to an increase in the balance of convertible notes outstanding during 2014 as compared to the 2013 period.

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Table of Contents*Other Income (Expense), Net*

Other income (expense), net decreased from \$6,000 in income for the three months ended March 31, 2013 to \$43,000 in expense for the three months ended March 31, 2014. This decrease resulted from a change in the fair value of the common stock warrant and preferred stock warrant liabilities.

Comparison of the Years Ended December 31, 2012 and 2013

The following table summarizes our results of operations for the periods indicated:

(in thousands)	YEAR ENDED DECEMBER 31,		INCREASE/ (DECREASE)
	2012	2013	
Government grant revenue	\$ 30	\$ 480	\$ 450
Operating expenses:			
Research and development	1,310	2,151	841
General and administrative	536	1,783	1,247
Total operating expense	1,846	3,934	2,088
Operating loss	(1,816)	(3,454)	(1,638)
Interest expense, net	(8)	(73)	(65)
Other income (expense), net	7	(96)	(103)
Change in fair value of embedded derivative	6	18	12
Loss on extinguishment of related party convertible notes	—	(1,671)	(1,671)
Net loss	<u>\$(1,811)</u>	<u>\$(5,276)</u>	<u>\$ (3,465)</u>

Revenue

Government grant revenue increased by \$450,000 from \$30,000 in 2012 to \$480,000 in 2013, due to our performance of an increased amount of reimbursed research under government grants in the 2013 period as compared to 2012.

Research and Development Expense

Research and development expense increased from \$1.3 million for 2012 to \$2.2 million for 2013. The increase in research and development expense was primarily due to an increase in clinical development costs incurred during 2013 for our clinical trials, including:

- \$0.2 million increase for clinical supply manufacturing and drug product process development activities in preparation for the AVA-101 clinical studies;
- \$0.3 million increase to contractor-related expenses to support the increased development activities in 2013;
- \$0.4 million increase in employee salaries and other personnel expenses as we increased our headcount during 2013;
- \$0.3 million increase in stock-based compensation expenses during 2013; and
- \$0.2 million increase in facilities expense during 2013.

The increase in research and development expense was partially offset by a reimbursement of \$0.8 million from the Australian tax authorities recorded as a reduction in research and development expense in 2013. For the years ended December 31, 2012 and 2013, substantially all of our research and development expense related to our development activity for AVA-101 for the treatment of wet AMD.

General and Administrative Expense

General and administrative expense increased \$1.2 million, from \$0.5 million in 2012 to \$1.8 million in 2013. The increase in general and administrative expense was primarily due to the recognition of \$0.8 million of collaboration acquisition costs related to the issuance of 689,455 shares of Series A convertible preferred stock to a potential collaborator for cash at a price per share below the fair value of such shares. We also experienced an increase in

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stock-based compensation and consulting and professional services expenses of \$0.5 million, and an increase in facility expense of \$0.2 million during 2013 as we expanded our operations.

Interest Expense

Interest expense increased by \$65,000 in 2013 as compared to the 2012 period. The increase was due to an increase in the balance of convertible notes outstanding during 2013 as compared to 2012.

Other Income (Expense), Net

Other income (expense), net for 2013 decreased \$0.1 million, from 2012 primarily due to a change in the fair value of the common stock warrant and preferred stock warrant liabilities.

Change in Fair Value of Embedded Derivative

We recorded an embedded derivative liability in connection with our 2012 Notes. We recorded change in the fair value of this derivative in our consolidated statements of operations and comprehensive loss. In November 2013, upon conversion of the 2012 Notes into Series A convertible preferred stock, the embedded derivative was terminated.

Loss on Extinguishment of Related Party Convertible Notes

In November 2013, we amended the terms of our existing 2012 Notes to accelerate their conversion into shares of Series A convertible preferred stock, which we determined represented an extinguishment. As a result, we recorded a loss on the extinguishment of convertible notes of \$1.7 million in 2013.

Liquidity, Capital Resources and Plan of Operations

Since our inception and through March 31, 2014, we have financed our operations through private placements of convertible notes and preferred stock with our investors, funding under our government grants and licensing revenue from an agreement related to the licensing of certain of our intellectual property, which we entered into during the first quarter of 2014. At March 31, 2014, we had cash of \$0.2 million. In April 2014, we received gross proceeds of \$52.9 million from the sale of Series B convertible preferred stock, of which \$4.0 million was used to repurchase outstanding shares of Series A convertible preferred stock from an existing investor. We also converted the outstanding balance under our 2012 Notes into shares of Series B convertible preferred stock. In May 2014, we received initial payments of \$8.0 million in connection with our research collaboration and license agreement with Regeneron. We expect that these funds, together with our existing cash as of March 31, 2014 will be sufficient to fund our operations through at least December 31, 2015.

We expect to incur substantial expenditures in the foreseeable future for the development and potential commercialization of our product candidates and ongoing internal research and development programs. In order to complete our planned preclinical and clinical trials and complete the process of obtaining regulatory approval for our lead product candidate, as well as to build the sales, marketing and distribution infrastructure that we believe will be necessary to commercialize our product candidates, if approved, we will require substantial additional funding.

We will continue to seek funds through equity or debt financings, collaborative or other arrangements with corporate sources, or through other sources of financing. Adequate additional funding may not be available to us on acceptable terms or at all. Our failure to raise capital in the future could have a negative impact on our financial condition and our ability to pursue our business strategies. We anticipate that we will need to raise substantial additional capital, the requirements of which will depend on many factors, including:

- the initiation, progress, timing, costs and results of clinical trials for AVA-101 and our other product candidates in development;
- the outcome, timing of, and costs involved in, seeking and obtaining approvals from the FDA and other regulatory authorities, including the potential for the FDA and other regulatory authorities to require that we perform more studies than those that we currently expect;
- the ability of our product candidates to progress through clinical development activities successfully;
- our need to expand our research and development activities;
- the rate of progress and cost of our commercialization of our products;
- the cost of preparing to manufacture our products on a larger scale;

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- the costs of commercialization activities including product sales, marketing, manufacturing and distribution;
- the degree and rate of market acceptance of any products launched by us or future partners;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- our need to implement additional infrastructure and internal systems;
- our ability to hire additional personnel;
- our ability to enter into additional collaboration, licensing, commercialization or other arrangements and the terms and timing of such arrangements; and
- the emergence of competing technologies or other adverse market developments.

If we are unable to raise additional funds when needed, we may be required to delay, reduce, or terminate some or all of our development programs and clinical trials. We may also be required to sell or license other technologies or clinical product candidates or programs that we would prefer to develop and commercialize ourselves.

Cash Flows

The following table sets forth the primary sources and uses of cash for each of the periods presented below:

(in thousands)	YEAR ENDED DECEMBER 31,		THREE MONTHS ENDED MARCH 31,	
	2012	2013	2013	2014
			(Unaudited)	
Net cash (used in) provided by:				
Operating activities	\$(1,267)	\$(2,175)	\$(144)	\$(1,347)
Investing activities	(3)	(91)	(78)	(47)
Financing activities	500	2,480	300	1,000
Net increase (decrease) in cash	<u>\$ (761)</u>	<u>\$ 207</u>	<u>\$ 79</u>	<u>\$ (395)</u>

Cash Used in Operating Activities

Net cash used in operating activities for the three months ended March 31, 2013 was \$0.1 million compared to \$1.3 million for the three months ended March 31, 2014. The increase was primarily due to an increase in our net loss from \$49,000 to \$1.7 million. The lower net loss for the three months ended March 31, 2013 is attributable to the receipt of reimbursement from the Australian tax authorities of \$0.5 million recorded as a reduction in research and development expense during the 2013 quarter. The net loss for the three months ended March 31, 2014 is attributable to higher external research and development costs associated with our company-sponsored clinical program, increased headcount and higher external consultants costs.

Net cash used in operating activities was \$1.3 million and \$2.2 million for 2012 and 2013, respectively. Cash used in operating activities in 2013 increased compared to 2012 primarily due to higher net loss from operations as we increased our research and development expenditures due to increased clinical trial activity during 2013.

Cash Used in Investing Activities

Cash used in investing activities consisted primarily of investment in property and equipment.

Cash Provided by Financing Activities

Cash provided by financing activities was \$0.3 million for the three months ended March 31, 2013, compared to \$1.0 million for the comparable period of 2014. Cash provided by financing activities for both periods consisted of proceeds from the issuance of related-party convertible notes.

Cash provided by financing activities was \$2.5 million for 2013, compared to \$0.5 million for 2012. Cash provided by financing activities for 2012 year consisted primarily of net proceeds from the issuance of convertible notes. Cash

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provided by financing activities for 2013 consisted of \$1.5 million from the borrowing under related-party convertible notes as well as \$1.0 million in net proceeds from the issuance of Series A convertible preferred stock in November 2013 to a potential collaborator.

Contractual Obligations and Commitments

We have lease obligations consisting of an operating lease for our operating facility that expires in 2019.

The following table summarizes our contractual obligations as of December 31, 2013:

(in thousands)	PAYMENTS DUE BY PERIOD				TOTAL
	LESS THAN 1 YEAR	1 TO 3 YEARS	4 TO 5 YEARS	AFTER 5 YEARS	
Lease obligations	\$ 120	\$ 571	\$ 631	\$ 441	\$1,763

We are obligated to make future payments to third parties under in-license agreements, including sublicense fees, royalties and payments that become due and payable on the achievement of certain development and commercialization milestones. As the amount and timing of sublicense fees and the achievement and timing of these milestones are not probable and estimable, such commitments have not been included on our balance sheet or in the contractual obligations tables above.

Off-Balance Sheet Arrangements

Since our inception, we have not engaged in any off-balance sheet arrangements, as defined in the rules and regulations of the SEC.

Quantitative and Qualitative Disclosures about Market Risk**Foreign Currency Exchange Risk**

A portion of our operating expenses are incurred outside the United States and are denominated in foreign currencies and are subject to fluctuations due to changes in foreign currency exchange rates, particularly changes in the Australian dollar. Additionally, fluctuations in foreign currency exchange rates may cause us to recognize transaction gains and losses in our statement of operations. To date, foreign currency transaction gains and losses have not been material to our consolidated financial statements, and we have not engaged in any foreign currency hedging transactions. As our international operations grow, we will continue to reassess our approach to managing the risks relating to fluctuations in currency rates.

Interest Rate Risk

We had cash of \$0.6 million and \$0.2 million as of December 31, 2013 and March 31, 2014, respectively, consisting of bank deposits that are not interest bearing. To date, fluctuations in interest income have not been significant. We also had total outstanding debt of \$1.0 million under our related-party convertible notes as of March 31, 2014, which were converted into shares of Series B convertible preferred stock in April 2014 in connection with the Series B convertible preferred stock financing.

We do not enter into investments for trading or speculative purposes and have not used any derivative financial instruments to manage our interest rate risk exposure. We have not been exposed to, nor do we anticipate being exposed to, material risks due to changes in interest rates. A hypothetical 10% change in interest rates during any of the periods presented would not have had a material impact on our consolidated financial statements.

We do not believe that inflation and change in prices had a significant impact on our results of operations for any periods presented in our consolidated financial statements.

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Table of Contents**BUSINESS****Overview**

We are a clinical-stage biotechnology company focused on discovering and developing novel gene therapies to transform the lives of patients with sight-threatening ophthalmic diseases. We have leveraged our next-generation gene therapy platform, the Ocular BioFactory™, to create a robust pipeline of product candidates. Our product candidates are designed to provide long-term benefit or a functional cure for these diseases by inducing a sustained expression of a therapeutic protein with a one-time administration in the eye.

We are targeting ophthalmic diseases with significant unmet medical need, including prevalent ophthalmic diseases such as wet age-related macular degeneration (AMD), as well as rare genetic diseases. We believe that there are several important benefits to focusing on the development of therapies for ophthalmic diseases, including the following:

- well-understood disease biology, in which many conditions are caused by a defect in expression of a single gene;
- reduced risk of harmful immune responses and systemic side effects due to localized delivery in a self-contained organ;
- relatively easy access and visualization of the back of the eye, limiting the need for invasive procedures to deliver therapies and evaluate their impact;
- well-defined and objective clinical endpoints such as the ability to read an eye chart; and
- significant market demand for therapies that can offer long-term clinical benefit with one-time administration.

Our lead product candidate is AVA-101 for the treatment of wet AMD. Standard-of-care therapies include the anti-VEGF class, which inhibit vascular endothelial growth factor (VEGF), a protein that causes abnormal blood vessel growth in wet AMD. Anti-VEGF therapies, such as Lucentis®, marketed by Genentech, Inc. and Novartis AG, and EYLEA®, marketed by Regeneron Pharmaceuticals, Inc. in the United States and Bayer HealthCare LLC outside the United States, represented over \$6.0 billion in worldwide sales in 2013, and we believe 65%-80% of those sales were for the treatment of wet AMD. Due to a variety of factors, including inconvenience and discomfort associated with frequent injections in the eye, patient compliance is a significant concern with anti-VEGF therapies. These treatments require continuous injections every four to eight weeks to maintain efficacy and patients often experience vision loss with reduced frequency of treatment. By contrast, AVA-101 is designed to enable retinal cells to continuously produce therapeutic levels of a naturally occurring anti-VEGF protein with a single administration. Accordingly, we believe that AVA-101 could transform the treatment paradigm and address a significant unmet need in this large wet AMD market. In addition to wet AMD, we believe that AVA-101 may have the potential to treat other neovascular diseases of the eye such as diabetic macular edema (DME) and retinal vein occlusion (RVO).

We have generated human proof-of-concept data for AVA-101 in a Phase 1 trial with eight wet AMD subjects conducted at LEI. In that Phase 1 trial, AVA-101 was well tolerated with no drug-related adverse events. In addition, subjects treated with AVA-101 showed meaningful improvement in their visual acuity test scores (up to 15 letter improvement on an eye chart from baseline), and most subjects did not receive any rescue injections of standard-of-care therapy (required for subjects exhibiting disease progression) during the one-year trial period.

We are currently conducting a Phase 2a trial for AVA-101 at LEI with 32 additional wet AMD subjects. Interim drug safety surveillance data received in June 2014 from this ongoing study suggests that AVA-101 continues to be well tolerated. Most adverse events that have been observed to date are mild and not related to AVA-101 or the procedures used in the study. Adverse events related to study procedures include subconjunctival, vitreous and retinal hemorrhage, cataract progression and eye pain. Other infrequent adverse events may be related to study procedures, including retinal tears or holes and falls. A small number of adverse events may be possibly related to AVA-101, including inflammation and light chain analysis increase, but these were considered mild and transient and have not been associated with vision loss. We expect to receive top-line data from this ongoing Phase 2a trial in mid-2015. We own exclusive rights to develop and commercialize AVA-101 worldwide.

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In addition to AVA-101, our Ocular BioFactory platform has generated other promising product candidates for the treatment of severe ophthalmic diseases, including:

- **AVA-201.** We are developing AVA-201 as a next-generation product candidate for the prevention of wet AMD. AVA-201 produces the same anti-VEGF protein as AVA-101 using a proprietary, customized delivery mechanism, or vector, that can be administered earlier in the disease progression, before the onset of wet AMD. According to the Center for Disease Control (CDC), up to 7.3 million patients in the United States are at high risk of developing wet AMD, and we believe that the highest risk patients can be identified through a combination of clinical and genetic biomarkers. These high-risk patients, if treated early enough in the disease progression, could potentially maintain their visual acuity instead of experiencing sudden onset of vision loss characterized by wet AMD. We own exclusive rights to develop and commercialize AVA-201 worldwide.
- **AVA-311.** As part of our research collaboration with Regeneron, AVA-311 is being evaluated in preclinical studies for the treatment of juvenile X-linked retinoschisis (XLRS), a rare genetic disease of the retina with no approved therapy. There are approximately 10,000 boys and young men in the United States suffering from the disease. XLRS is caused by mutation of the RS1 gene and results in splitting of retinal layers and corresponding loss of vision. In preclinical studies in animals to date, AVA-311 has delayed the progression of XLRS and improved vision by delivering functional copies of the RS1 gene in retinal cells of mice.

In order to accelerate the pace of generating and developing product candidates for our pipeline, we entered into a broad research collaboration and license agreement (Collaboration Agreement), with Regeneron in May 2014. Under the terms of the collaboration, we will jointly discover novel product candidates based on our Ocular BioFactory platform for up to eight therapeutic targets including AVA-311. We received initial payments of \$8.0 million as well as ongoing support for research and development. In addition, we are eligible to receive up to \$80.0 million in development milestone payments for product candidates directed toward each therapeutic target, for a combined total of up to \$640.0 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, and low- to mid-single-digit royalties on worldwide net sales of collaboration product candidates. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits. See "License and Collaboration Agreements—Regeneron Research Collaboration and License Agreement" for more information regarding our collaboration agreement.

Our Ocular BioFactory platform seeks to treat the cause of ophthalmic diseases by enabling patients' own cells to express a therapeutic protein for a sustained period of time. We use a vector derived from adeno-associated virus (AAV), which is a small, non-pathogenic virus. DNA encoding the AAV viral genes are removed and replaced with a therapeutic gene to treat a disease. The resulting vector is used to deliver and express, or transduce, a functional gene to the cells of the eye to promote continuous protein production. Although AAVs are widely used for gene therapy due to their safety, stability and sustained protein expression, our Ocular BioFactory platform has distinct characteristics that provide advantages over competing gene therapy technologies using AAVs as well as other viral and non-viral vectors.

Our Ocular BioFactory platform features two key proprietary components: a vector screening and optimization system referred to as directed evolution, and an industrialized manufacturing process. Through directed evolution, we generate a diverse library of millions of AAV variants and subsequently screen the variants in multiple *in vitro* and *in vivo* tests to identify the optimal variant for a specific disease. Our directed evolution technology allows us to create proprietary vectors and optimize them to target cells in different layers of the retina. Each of these cell layers constitutes a potential therapeutic target for currently unmet medical needs, providing us with multiple opportunities to apply our directed evolution technology. Our industrialized manufacturing process, based on our proprietary system, is highly efficient and stable. It uses the baculovirus expression system (BVES), which is a technology for producing high levels of recombinant protein in insect-derived cells. Production yields are more than 50 times greater than those obtained using conventional AAV production systems. Therefore, we are able to manufacture commercial grade production for large markets such as wet AMD.

Our senior management team and board of directors have significant experience in the biotechnology industry, specifically in the areas of ophthalmology and gene therapy. Our Chief Executive Officer and co-founder, Thomas W. Chalberg, Jr., Ph.D., was a member of the ophthalmology team at Genentech that was responsible for the successful

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launch and commercialization of Lucentis. Furthermore, Dr. Chalberg was a Howard Hughes Medical Institute Fellow at Stanford University, where his research focused on retinal diseases and novel technologies for gene therapy.

Our Chairman and co-founder, Mark S. Blumenkranz, M.D., is an ophthalmologist, a trained vitreoretinal surgeon and the Chairman of the Byers Eye Institute at Stanford University. Dr. Blumenkranz was also a founding member of the Eyetech Scientific Advisory Board. Dr. Blumenkranz also serves on the boards of directors of Vantage Surgical Systems Inc., Oculogics, Inc., Presbia Holdings, Digsight Technologies Inc. and Oculeve, Inc.

Our director and co-founder, Steven D. Schwartz, M.D., is an ophthalmologist and a trained vitreoretinal surgeon at the UCLA Jules Stein Eye Institute, where he has served as principal investigator in a number of early-stage clinical trials for retinal diseases, including the initial studies for Lucentis and novel product candidates in gene and cell therapy. Dr. Schwartz held various key positions at Eyetech, and has served on a number of Scientific Advisory Boards, including Genentech and Ophthotech Corporation.

Other members of our executive management team also have significant experience in the discovery and development of gene therapies including, expertise and/or prior experience at gene therapy companies in the following areas: regulatory, led by Samuel Barone, our Chief Medical Officer with prior experience at the Office of Cellular, Tissue and Gene Therapies at the Food and Drug Administration (FDA); manufacturing, led by Mehdi Gasmi, our Vice President, Pharmaceutical Development, with prior experience at Ceregene, Inc. and Génethon; finance, led by Linda Bain, our Chief Financial Officer with prior experience at bluebird bio, inc., Genzyme Corporation and AstraZeneca plc; and IP strategy, led by Hans Hull, our Senior Vice President, Legal and Corporate Development, with prior experience at Second Genome, Inc. and Aprelia Pharmaceuticals Company and as an attorney at Heller Ehrman White & McAulliffe LLP.

Strategy

Our goal is to transform the lives of patients suffering from blinding and sight-threatening diseases by discovering, developing and commercializing potentially curative therapies. The key elements of our strategy to achieve this goal are to:

- **Successfully advance AVA-101 through clinical development and commercial launch for wet AMD.** Global sales of Lucentis and EYLEA were over \$6.0 billion in 2013 with approximately \$3.3 billion in the United States and \$2.8 billion in territories outside of the United States, of which we believe a significant portion occurred in the European Union, Japan and Australia. We believe 65%-80% of those sales were for the treatment of wet AMD. We intend to pursue a worldwide development and commercialization strategy of advancing AVA-101 in the United States and these international markets. After the completion of our Phase 2a clinical trial in mid-2015, we plan to file an IND in the United States and work with regulatory authorities to pursue a global regulatory strategy. We currently own worldwide rights to AVA-101. Given the small number of retina specialists globally, we believe we will have the opportunity to commercialize AVA-101 alone or with a partner. We will pursue a commercialization strategy that will increase the probability of AVA-101's ultimate success and maximize value for our shareholders.
- **Pursue additional indications for AVA-101.** There are other diseases in which VEGF plays a central role in disease biology, including DME and RVO. Anti-VEGF therapies such as Lucentis and EYLEA are already approved in these indications. Since patient compliance presents the same challenge in these indications, we believe that AVA-101 may offer an attractive alternative to the existing therapies in these markets.
- **Continue to identify and target ophthalmic diseases using our Ocular BioFactory platform.** We are focusing on both prevalent and rare ophthalmic diseases for which the disease biology is well characterized and for which the diseases themselves can be better treated by the sustained delivery of a therapeutic protein. These diseases include choroideremia, diabetic retinopathy, glaucoma, Leber's congenital amaurosis (LCA), macular telangiectasia, retinitis pigmentosa, wet AMD and XLRs, among others. We will continue to identify the most appropriate target indications based on emerging data from our platform, by leveraging our internal expertise and through relationships with thought leaders in ophthalmology.
- **Continue to invest in our Ocular BioFactory platform.** Our Ocular BioFactory platform has been validated by both preclinical and clinical data from our product candidates. We will continue to invest in our platform and employ directed evolution to create and manufacture next-generation vectors with higher efficiency and

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greater specificity that can potentially treat previously untreatable diseases. We believe this new class of therapeutics could emerge as a major treatment modality for ophthalmic diseases.

- **Build a balanced portfolio of proprietary and partnered programs.** We plan to develop and commercialize multiple product candidates independently. For targets outside our core area of interest or where a partner can contribute specific expertise, we intend to evaluate collaborations with strategic partners who can augment our industry-leading expertise in gene therapy for the eye. For example, in May 2014, we entered into a collaboration with Regeneron to leverage our Ocular BioFactory platform to discover and develop product candidates focused on up to eight therapeutic targets.

Gene Therapy Background

Gene therapy is a powerful treatment modality to address disease biology in a targeted and efficient way. Using gene therapy, physicians can introduce or re-introduce genes that encode a therapeutic protein. Instead of providing proteins or other therapies externally and dosing them over a long period, gene therapy offers the possibility of dosing once or a very limited number of times to achieve a long-term, durable benefit. Once a patient's cells have incorporated the therapeutic gene, the cells are able to continue to produce the therapeutic protein for years or, potentially, the rest of the patient's life.

Similar to existing classes of protein or biologic therapies such as monoclonal antibodies and drug-antibody conjugates, gene therapy has taken a number of years to evolve from a research tool into a viable and compelling treatment modality. There have been several recent advances in gene therapy, including the following:

- **Clinical data.** Positive data from gene therapy have been reported in a variety of indications including adrenoleukodystrophy, beta-thalassemia, chronic lymphoid leukemia, hemophilia, HIV and Parkinson's disease, as well as several ophthalmic diseases such as LCA and wet AMD.
- **Increased investment by biopharmaceutical companies.** The modality of gene therapy has been further validated by growing interest and investments by biopharmaceutical companies. Large, global biopharmaceutical companies, such as BioMarin Pharmaceutical Inc., Celgene Corporation, GlaxoSmithKline plc, Novartis, Sanofi, Regeneron, and Shire Pharmaceuticals Group Plc, have increased their investment in the gene therapy field. Additionally, pure-play gene therapy companies, such as Applied Genetic Technologies Corporation, bluebird bio, Celladon Corporation, Sangamo BioSciences, Inc. and uniQure N.V., have attracted recent investment in this growing field.
- **Regulatory clarity.** Although the FDA has not yet approved a gene therapy product, it has provided guidance for the development of gene therapy products. For example, the FDA has established the Office of Cellular, Tissue and Gene Therapies within CBER to consolidate the review of gene therapy products, and the Cellular, Tissue and Gene Therapies Advisory Committee to advise CBER on its reviews.
- **First product approval.** In 2012, the EMA granted approval for Glybera® (developed by uniQure) for the orphan disease lipoprotein lipase deficiency. Glybera is the first gene therapy product approved in the Western world.

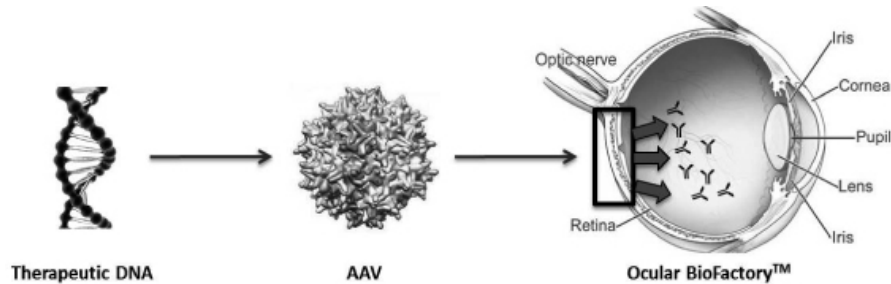
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[Table of Contents](#)**Our Ocular BioFactory Platform**

Our Ocular BioFactory platform seeks to treat the cause of ophthalmic diseases by enabling patients' own cells to express a therapeutic protein for a sustained period of time. Our proprietary Ocular BioFactory platform features three key attributes: focus on the treatment of serious ophthalmic diseases; novel AAV vector discovery and optimization system; and our industrialized manufacturing process.



When injected into the eye, AAV creates a long-term Ocular BioFactory that secretes therapeutic protein over years following a single administration

Focus on the Treatment of Serious Ophthalmic Diseases

We believe that there are several important benefits to focusing our Ocular BioFactory platform on the development of therapies for ophthalmic diseases. These benefits include the following:

- **Unmet need.** There is a significant unmet medical need for patients suffering from various blinding or sight-threatening ophthalmic diseases. In certain degenerative eye diseases, such as wet AMD, there are effective therapies targeting factors established to be important in disease progression. However, the effectiveness of these therapies is limited by poor compliance due to the need for regular injections into the eye. For many rare genetic ophthalmic diseases, including XLRS, there are no approved therapies. In these diseases, serious sight-threatening symptoms arise early in patients' lives.
- **Well-understood disease biology.** Many ophthalmic diseases are caused by a defect in expression of a single gene or a small number of genes and the molecular mechanisms are well understood. As a result, in many cases, highly predictive animal models are available for these disease states, which allow us to obtain proof-of-concept data for product candidates early in development.
- **Safety.** The eye is a small, self-contained organ, separated from the rest of the body by physical and biochemical barriers. Therefore, drugs delivered into the eye are much less likely to evoke a systemic immune response. Gene therapies can be delivered locally at concentrations that are highly effective in the eye and at the same time lead to little or no systemic distribution.
- **Accessibility.** The eye is easily accessible for treatment, in contrast to internal organs that can be accessed only via the bloodstream or by invasive procedures. Furthermore, the retina and surrounding structures can be visualized and targeted by clinicians in a non-invasive and localized manner, making it easy to evaluate both the delivery of therapy as well as its impact.
- **Well-defined and accepted clinical endpoints.** Clinical endpoints for ocular disease generally consist of objective, well-defined, performance-based parameters such as the ability to read an eye chart. These endpoints have been used for many years and are well understood and accepted by clinical investigators, regulatory agencies and practicing ophthalmologists.

Our Novel AAV Vector Discovery and Optimization System

Our Ocular BioFactory platform is based on AAV vectors, which offer numerous advantages over other viral and non-viral vector technologies used for gene therapy. These advantages, highlighted below, allow AAVs to be safe, applicable for a variety of indications and to exhibit long-term efficacy.

- **Non-pathogenic.** AAV vectors are not known to cause any disease in humans.

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- **Low immunogenicity.** AAV vectors elicit only a mild immune response, if any, in humans, particularly when used in the eye.
- **Non-replicating.** Once inside the host cell, AAV vectors do not replicate, thereby preventing the spread to unwanted tissues.
- **Non-integrating.** AAV vectors do not readily integrate into the host cell's genome, mitigating the risk of potential safety concerns.
- **Ability to transduce non-dividing cells.** AAV vectors are able to transduce non-dividing cells and this is a significant advantage as many retinal cells cease to divide early in a person's life.
- **Long-term expression.** Once incorporated into the host cell, AAV vectors can continue to drive expression of a therapeutic protein for years.

AAV is naturally occurring and has become a leading vector used in gene therapy. According to the *Journal of Gene Medicine*, AAV has been used in approximately 100 clinical trials as of January 2014 demonstrating the increasing acceptance of gene therapy as a safe and effective method for delivering therapeutic genes of interest. The most frequently studied variant of AAV is AAV2, which can preferentially infect a number of cell types, including those found in the retina. AAV2 is the basis for our lead product AVA-101.

As effective as existing AAV vectors are in gene therapy, we believe there is an opportunity to advance vector capabilities beyond those currently available. Naturally occurring AAV variants have evolved with particular characteristics, some of which pose limitations to their use in gene therapy in the eye. Consequently, there is significant room to improve AAV vectors to maximize utility for gene therapy in the eye. Therefore, our other product candidates have been created using our methodology that gives AAV new and powerful capabilities of cell penetration, gene delivery, protein expression and manufacturability. We believe we can target retinal cells even more precisely with these next-generation AAV vectors, to one or more of the eight cell layers found in the retina.

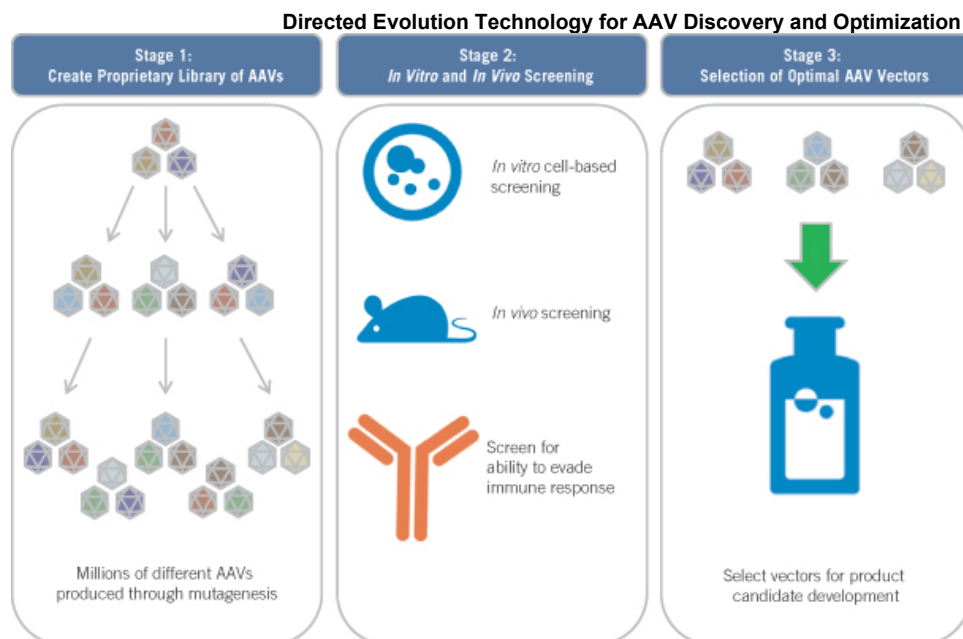
In order to create next-generation vectors, we use a multi-step process known as directed evolution. These vectors are designed to penetrate a specific cell type within the retina with high efficiency and transduce cells to express a therapeutic protein over a long duration.

Our directed evolution technology uses a library of genes coding for viral proteins found in a number of naturally occurring AAVs. We modify these genes in the laboratory to derive novel combinations of genes that produce vectors exhibiting different properties and capabilities. Once we have created an initial pool of millions of different AAVs, each with distinct genetic and chemical composition, we screen the AAVs in the pool for their potential therapeutic benefits. We also screen the pool to eliminate vectors that would lead to interference by a host's antibodies. After identifying a smaller pool of optimized vectors from this screening process, we repeat the steps of diversity generation and screening until we have identified a select number of ideal, engineered AAVs. These lab-created AAVs represent the basis for our therapeutic product pipeline. Furthermore, when we develop additional product candidates, we return to the initial pool of novel vectors, or to one or more of the adapted pools we created, and use further applications of directed evolution to create new AAVs.

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Developing next-generation AAV vectors through directed evolution allows us to develop gene therapy product candidates that are able to enter the desired cell populations. Once the genes have been transduce the appropriate cells, our product candidates can increase or initiate the production of therapeutic proteins in physiologically relevant amounts. Our directed evolution technology provides us with a toolkit to create AAV-based product candidates that we believe will be able to address any number of common and rare ophthalmic diseases.

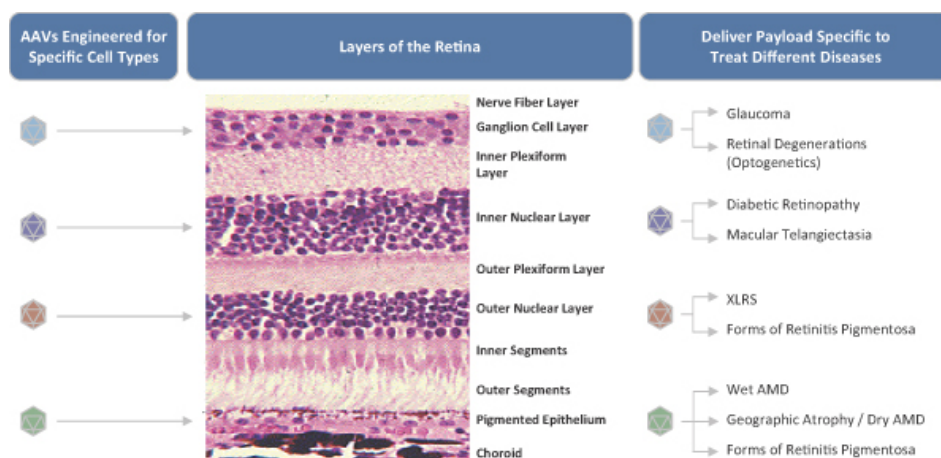


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Table of Contents**Our Industrialized Manufacturing Process**

Our AAV manufacturing method is industrialized, ready for adaptation to commercial processes and highly scalable. It is based on the BVES, which has been used in a number of FDA- and EMA-approved products. Our process provides the following advantages over competing systems:

- **Industrial-scale biologics production.** Our BVES system can produce commercial quantities by incorporating scalable, well-established process steps used throughout the industry for biologic products.
- **Safety advantages.** Our BVES system does not use mammalian cell cultures or tumorigenic cell lines, and the DNA sequences used in production are inactive in mammalian cells, which lowers the risk of off-target expression from our products.
- **High yield and low cost.** Our BVES system produces a high number of particles per cell, producing many thousand doses per manufacturing run. The yields are up to one hundred times greater than those obtained using conventional AAV production systems. This lowers the unit cost of goods, allowing us to meet global demand for large markets, such as wet AMD.
- **High purity.** Our BVES system produces a highly pure drug substance, which reduces the presence of unwanted contaminants in the final product.
- **Precedent regulatory framework.** Our BVES system is used for several FDA- and EMA-approved vaccines and gene therapy products including FluBlok®, Cervarix® and Glybera.

Our Product Candidates

Based on our Ocular BioFactory platform, we have developed a robust pipeline of proprietary and partnered programs across both major markets and rare diseases in the field of ophthalmology. Set forth below is a table summarizing our development programs:

Product Candidate	Indication	Stage of Development			Near-term Milestones	Worldwide Commercial Rights
		Research	Preclinical	Phase 1 / 2		
AVA-101	Wet AMD				<ul style="list-style-type: none">■ Top-line Phase 2a data expected mid-2015■ IND filing 2H 2015	Avalanche
AVA-101	DME and RVO				<ul style="list-style-type: none">■ IND-enabling studies planned for 2014 and 2015	Avalanche
AVA-201	Wet AMD (Prevention)				<ul style="list-style-type: none">■ Preclinical studies in 2014 and 2015	Avalanche
AVA-311	XLRS					Regeneron; Avalanche receives milestones and royalties and has an option to share development costs and profits

Broad Research Collaboration with Regeneron for up to 7 Additional Targets

AVA-101 for the Treatment of Wet AMD

We are developing our lead product candidate, AVA-101, to provide a safe and effective treatment for wet AMD that is durable and reduces the need for frequent injections. AVA-101 is currently being studied in a 40 subject Phase 1/2a trial that we are conducting together with LEI. One-year results from the Phase 1 portion (eight subjects) have been reported. The Phase 2a trial (32 subjects) is fully enrolled, and top-line data are expected in mid-2015.

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We own exclusive rights to develop and commercialize AVA-101 worldwide. Regeneron has a time-limited right of first negotiation for certain rights to AVA-101 as part of our recent collaboration.

Wet AMD Overview

AMD is a progressive disease affecting the retinal cells in the macula, the region of the eye responsible for central vision. Disease progression results in the death of retinal cells and the gradual loss of vision. As people age, the likelihood of disease progression increases and the resulting condition is referred to as AMD.



Approximately 10% of total cases of AMD represent an advanced form of the disease called wet AMD, in which blood vessels begin to invade the cellular space between layers of cells in the retina. These new blood vessels are often leaky, which results in fluid and blood in the retina and causes vision loss.

While wet AMD represents only 10% of the number of cases of AMD overall, it is responsible for 90% of the AMD-related severe vision loss. Of untreated patients who are not already partially sighted or blind, over half will become partially sighted or blind within three years.

Wet AMD is a leading cause of vision loss with a prevalence of approximately three million people worldwide. The incidence of new cases of wet AMD in the United States is approximately 150,000 to 200,000 a year and this number is expected to grow significantly based on the aging of the population.

Current Therapies for Wet AMD

While the underlying molecular causes of AMD are not completely known, VEGF is known to play a central role in the growth of new blood vessels in wet AMD. A number of therapies have been developed to block the effects of VEGF by binding to and sequestering the protein. The standard-of-care therapies include the following:

- Lucentis is a recombinant humanized monoclonal antibody fragment that binds to and inhibits VEGF proteins in the eye. This product was approved in the United States in 2006 and in Europe in 2007. In 2013, Lucentis achieved worldwide sales of \$4.3 billion.
- EYLEA is a recombinant fusion protein containing portions of the human VEGF receptor that binds to soluble VEGF. Approved in the United States in 2011, EYLEA has exhibited strong adoption in the market due to its more convenient dosing regimen compared to Lucentis. In 2013, EYLEA achieved worldwide sales of \$1.9 billion.
- Avastin is a recombinant human monoclonal antibody that binds to VEGF and is approved as an anti-cancer agent. Avastin is widely prescribed off-label in ophthalmic diseases such as wet AMD. Avastin makes up approximately 60% of the wet AMD market by volume, but is insignificant in terms of revenue.

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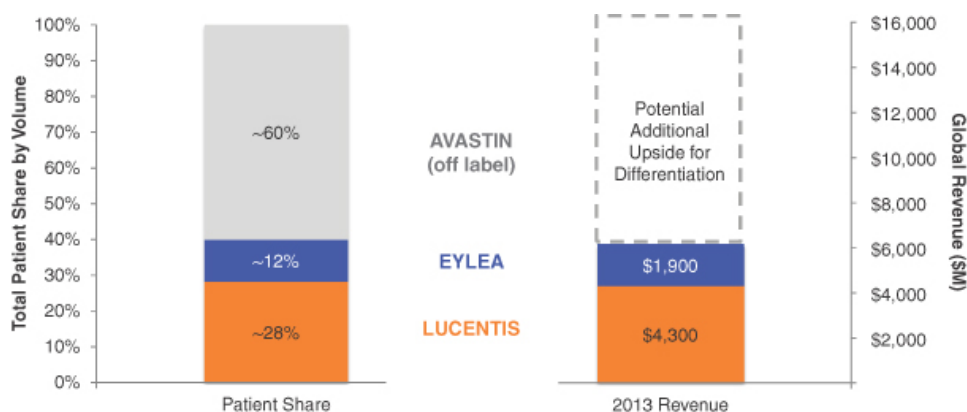
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We believe a novel therapy that represents a functional cure is meaningfully differentiated from standard-of-care therapies and will have access to the entire wet AMD market, not just the 40% treated with on-label Lucentis and EYLEA, but also the large pool of patients currently using Avastin off-label.

Comparison of Patient Share Volume and Global Revenues for Anti-VEGF Therapies



While standard-of-care treatments have proven to be effective, they do not offer a durable remission and require injections into the patient's eye every four to eight weeks. According to the journal *Ophthalmology* (2012), in the MARINA and ANCHOR trials (conducted by Genentech), a total of 599 subjects received Lucentis every four weeks. Treated subjects in these trials gained vision, averaging 9.0 letters on a standardized eye chart, and this gain was maintained with injections every four weeks for two years. When 388 of these subjects were subsequently moved to a less-frequent dosing regimen in the HORIZON study (Genentech), however, their vision declined by 7.0 letters over the next two years. In the SEVEN-UP study reported in the journal *Ophthalmology* (2013), 65 subjects from the HORIZON study were followed for an additional 3.3 years and injected less frequently, declining by an additional 10.3 letters.

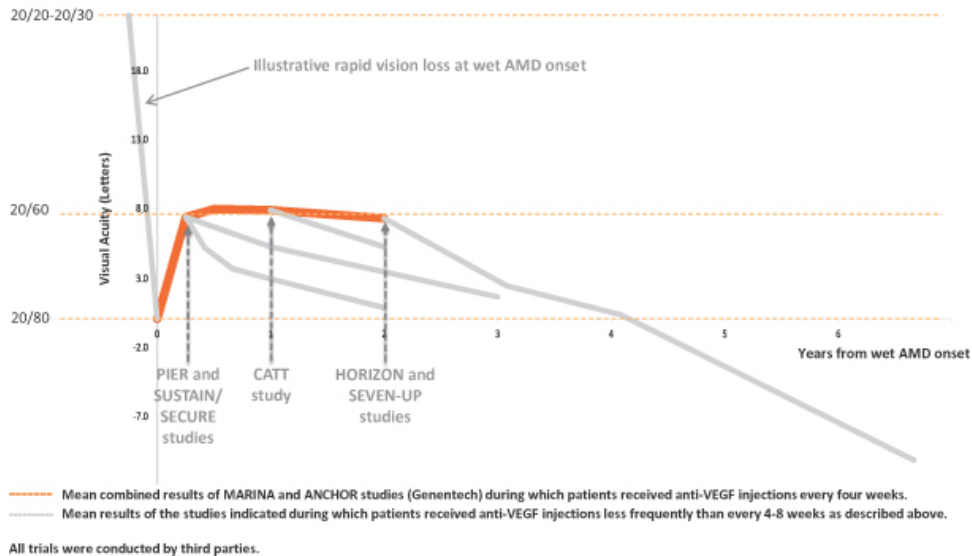
Other clinical trials where subjects were treated less frequently than every 4 weeks have shown similar results. In the PIER study (Genentech), 61 subjects received three doses every 4 weeks, gaining 4.3 letters, but were then switched to 12-week dosing and declined 6.5 letters at two years (British Journal of Ophthalmology, 2009). In the SUSTAIN study (Novartis), 512 subjects received three doses every 4 weeks, gaining 5.8 letters, but were then switched to less frequent "as needed" dosing, and declined 2.2 letters at 12 months (*Ophthalmology*, 2011); 99 of these subjects continued to be followed in the SECURE study (Novartis) and were treated with less frequent "as needed" dosing and lost an additional 3.6 letters (*Ophthalmology*, 2013). Similarly, in CATT (United States National Eye Institute), 130 subjects were dosed monthly for 12 months, gaining 8.5 letters (*New England Journal of Medicine*, 2011), but then were switched to less-frequent "as needed" dosing and declined by 1.8 letters.

As summarized in the illustrative chart below, patients must comply with a burdensome treatment regimen every 4-8 weeks, or face a relative decline in visual acuity. The chart depicts the results for the MARINA and ANCHOR studies, compared to the decline in visual acuity from less frequent dosing in the other studies, as described above. When injections are given every four weeks, as in the MARINA and ANCHOR studies, patients initially gain vision and maintain that gain. However, when patients were relieved of injections every four weeks after three months (PIER and SUSTAIN/SECURE trials), twelve months (CATT trial), or two years (HORIZON and SEVEN-UP trials), the results were similar.

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Despite sub-optimal outcomes with injections less than every four to eight weeks, patients often terminate treatment or do not comply with the prescribed regimen due to the burdensome frequency of administration. According to the *European Journal of Ophthalmology* (2011), 36% of patients who received anti-VEGF treatment for at least six months had stopped receiving therapy within a year. Of these patients, 59% had lost visual acuity. In addition, according to the journal *Ophthalmology* (2013), a study of a subset of 65 patients enrolled in Lucentis pivotal trials reported that only 23% of patients received more than 11 anti-VEGF treatments over the course of five years following the completion of the original trial. 59% of patients in this trial received fewer than six anti-VEGF injections during the follow up period and they lost an average of 9.3 letters of visual acuity. Studies examining treatment patterns in the real world report that patients are substantially under-treated, receiving an average of only five to seven injections per year; over time, this under-treatment has persisted despite evidence of worse visual outcomes (*American Journal of Ophthalmology*, 2014).

Our Solution: AVA-101

AVA-101 is comprised of the AAV2 vector, which contains a gene encoding sFLT-1, a naturally occurring anti-VEGF protein. When administered in the eye and expressed by the host retinal cells, the sFLT-1 protein inhibits the formation of new blood vessels and reduces vascular permeability by binding and blocking VEGF activity.

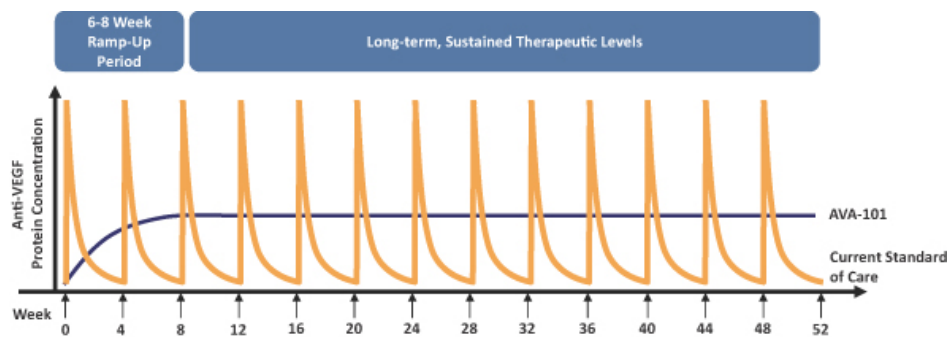
AVA-101 is designed to be administered via a single subretinal injection. The vector is placed into direct contact with retinal cells, which then produce sFLT-1. We believe that a majority of vitreoretinal surgeons are capable of performing the procedure to deliver AVA-101, which is an outpatient procedure performed under local anesthesia.

Based on data from preclinical studies, AVA-101 reaches a therapeutically beneficial level of continuous expression of sFLT-1 within six to eight weeks from administration. In animal models, AVA-101 expression has been shown to last up to 17 months, and data from other studies with AAV in the retina have shown gene expression to last more than five years. In humans, AVA-101 has been studied up to one year, and we believe it has the potential to last much longer.

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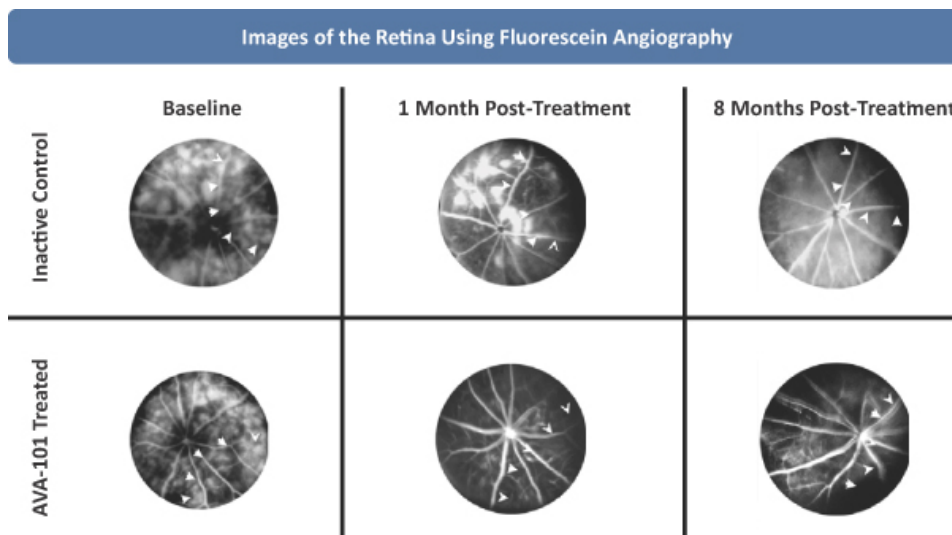
Table of Contents**Sustained Expression of sFLT-1 for AVA-101 Compared to Current Standard of Care**

Above is an illustration of how our AVA-101 approach is designed to produce steady and sustained expression of sFLT-1 compared to the peaks and troughs experienced by patients on the current standard of care.

AVA-101 Preclinical Studies

Multiple preclinical studies of AVA-101 demonstrated no vector-specific adverse effects. For example, a study in 45 mice did not identify any systemic immune response subsequent to subretinal injections; the localized immune response in treated eyes was mild and transient and did not interfere with long-term efficacy or safety.

Highlighted below are results from a transgenic mouse model of wet AMD for AVA-101. The study demonstrated that the retinal neovascular lesions, a model for wet AMD, improved following treatment with AVA-101. An examination of eye tissues treated with AVA-101 also revealed that photoreceptors were preserved as compared to controls.

AVA-101: Transgenic Mouse Neovascularization Model

Transgenic mice expressing VEGF show symptoms of retinal neovascularization, including hyperpermeability, retinal degeneration, and scarring. Mice were treated with an inactive control vector (top row) or AVA-101 (bottom row) in the area demarcated by arrowheads. Mice treated with AVA-101 showed reduced neovascularization and scarring compared to those treated with an inactive control vector.

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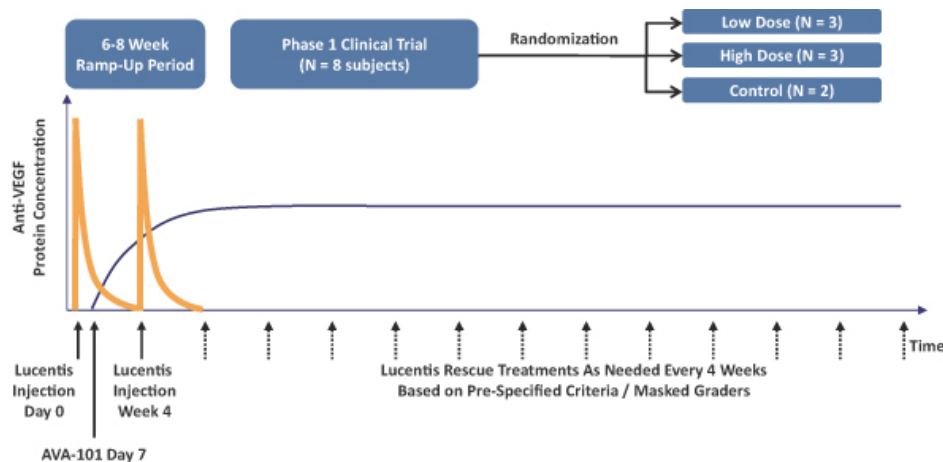
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We are evaluating AVA-101 in a Phase 1/2a trial at LEI in Australia. The Phase 1 portion involving eight subjects completed the twelve-month endpoint and data has been reported. The Phase 2a portion involving 32 subjects is fully enrolled with top-line data expected in mid-2015.

The goal of the Phase 1 trial was to establish initial ophthalmic and systemic safety, as well as to investigate early efficacy as defined by improvement in visual acuity, reduction in retinal thickness and a reduced number of anti-VEGF (Lucentis) rescue injections. Participation in the trial was limited to subjects 55 years or older with confirmed neovascular leakage associated with AMD. Subjects were randomized into three groups: control, low AVA-101 dose (10^{10} vector genomes) and high AVA-101 dose (10^{11} vector genomes). All subjects received two initial doses of Lucentis at Day 0 and Week 4 and the subjects in the active arms received AVA-101 on Day 7. Beginning with the Week 8 visit, Lucentis was given as rescue therapy on an as-needed basis. The requirement for rescue therapy was based on objective criteria of disease recurrence as judged by personnel that were unaware of the subjects' treatment group. Subjects were assessed every four weeks for adverse events, retinal thickness, visual acuity and the need for Lucentis rescue injections.

AVA-101 Phase 1 Illustrative Trial Design

All subjects received two initial doses of Lucentis on Day 0 and Week 4 and the subjects in the active arms received AVA-101 on Day 7. Beginning with the Week 8 visit, Lucentis was given as rescue therapy on an as-needed basis.

One-year follow up from the Phase 1 portion of the trial was completed in April 2012. No significant drug-related safety concerns were observed. There were mild and transient inflammatory responses related to the injection, but no effects that were deemed to be drug-related. There were no clinically significant adverse events detected systemically by clinical tests and no systemic anti-VEGF related events. The AAV vector was not detected outside of the treated eye.

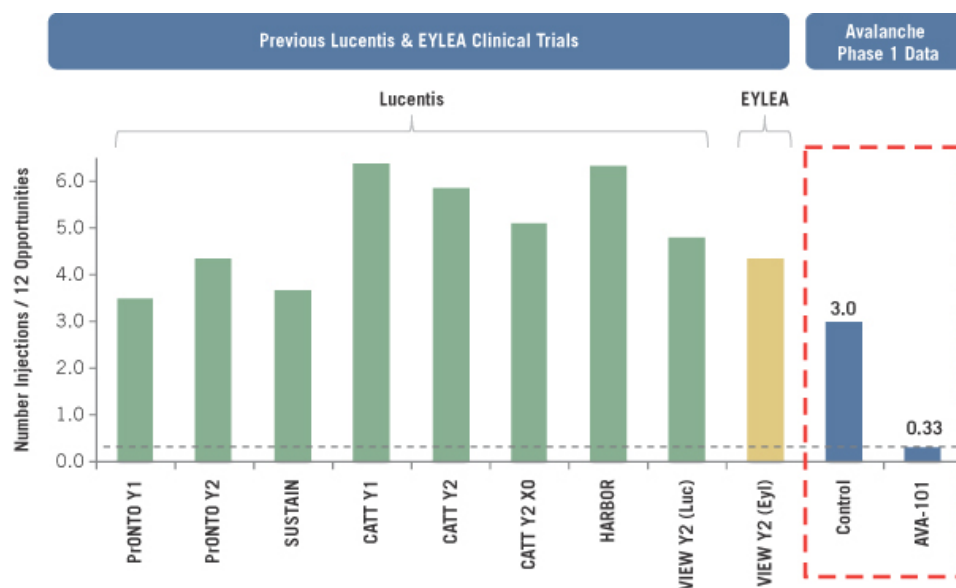
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Based on data from several previous clinical trials of Lucentis and EYLEA, when subjects are seen every four weeks and treated only as needed, they receive injections at 29% to 52% of visits. This translates to 3.5 to 6.4 injections out of 12 opportunities. In our Phase 1 trial, the control subjects needed 3.0 rescue treatments during the 12 opportunities from Week 8 to Week 52. By contrast, subjects receiving low or high dose of AVA-101 needed an average of only 0.33 rescue treatments over the same period. This equates to four of the six subjects in the active arms requiring no rescue injections, and two of the six subjects in the treatment arms requiring only a single rescue injection.



As shown in the graph below, the average retinal thickness for all subjects treated with AVA-101 decreased meaningfully and this effect was maintained for the entire year of the trial.

AVA-101 Phase 1: Average Change in Retinal Thickness of Treated Subjects

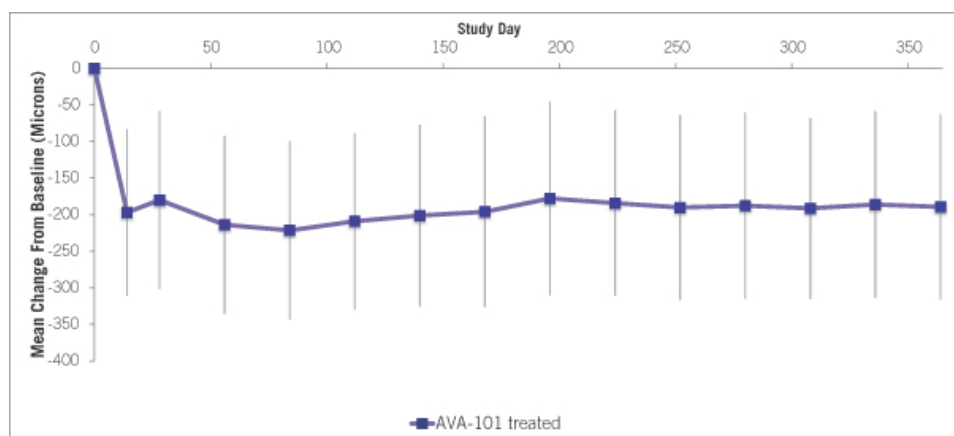


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As highlighted in the table below, visual acuity improved in the high and low dose AVA-101 treated groups by an average of 8.7 and 6.3 letters from baseline, respectively. Despite an average of three extra injections of Lucentis, the control subjects lost 3.5 letters of visual acuity. Five of six subjects improved ≥ 5 letters from baseline, and three of six subjects improved ≥ 10 letters. One subject lost six letters from baseline; this subject had significant sub-foveal scarring at baseline, and consequently may not have had the ability to improve. Such subjects will be excluded from future trials designed to evaluate the efficacy of AVA-101.

AVA-101 Phase 1: Change in Visual Acuity

Group	Subject	Baseline Visual Acuity (ETDRS Letters)	Week 52 Visual Acuity (ETDRS Letters)	Change from Baseline	Change from Baseline
Low Dose	R1001	33	40	+7	+8.7
	R1002	28	41	+13	
	R1004	46	52	+6	
High Dose	R2005	56	50	-6	+6.3
	R2006	54	64	+10	
	R2008	34	49	+15	
Control	R1003	28	21	-7	-3.5
	R2007	39	39	+0	

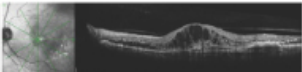
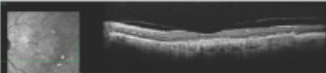
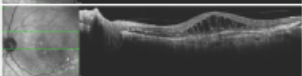
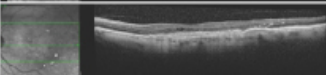
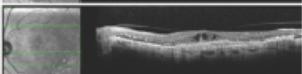
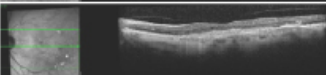
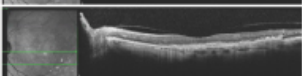
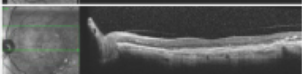
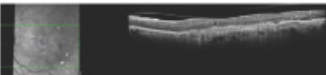
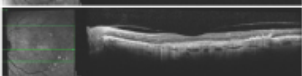
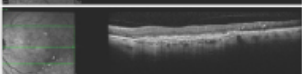
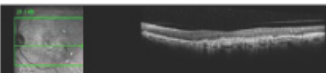
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Table of Contents**Case Study of Subject Treated with AVA-101**

The table below depicts one example of the therapeutic benefit of AVA-101 in the Phase 1 trial. This subject exhibited an advanced form of wet AMD, having received 24 injections of Lucentis prior to enrolling in the trial and with a visual acuity (VA) score of 26 at screening and 28 at baseline (approximately 20/250 on the Snellen scale). As evident from the scan below, the retina contained significant fluid, leading to increased retinal thickness. Pursuant to the trial protocol, the subject received Lucentis during the ramp-up phase on Day 0 and Week 4 and received one injection of low-dose AVA-101 on Day 7. By Week 8, the subject showed improved retinal anatomy and seven letter improvement in visual acuity. By Week 52, the subject's visual acuity increased by 13 letters from baseline to approximately 20/150 on the Snellen scale. In addition, the subject did not require a single rescue treatment of Lucentis following Week 4 throughout the duration of the trial.

Week	VA		Week	VA	
scr	26		24	37	
bsl	28		28	42	
4	22		32	40	
8	35		36		
12	40		40	35	
16	37		44	43	
20	30		48	44	
			52	41	

Clinical Development for AVA-101

We initiated the Phase 2a portion of this trial in 32 subjects in August 2012. The trial design is similar to the Phase 1 trial. This portion of the study included subjects with less advanced disease compared to the Phase 1 subjects, including less extensive scarring and visual acuity up to 20/30. Subjects were randomized 2:1 to high dose AVA-101 and control with similar ramp up and re-treatment criteria as in the Phase 1 portion. The primary endpoint is safety and secondary endpoints include retinal thickness, visual acuity and the need for rescue injections with anti-VEGF therapy (Lucentis). The trial is fully enrolled and we expect to report top-line data in mid-2015.

Following the ongoing Phase 2a study, we plan to file an IND in the United States. Subsequently, we plan to conduct a Phase 2b trial in the United States in the second half of 2015. The planned trial will be a randomized, controlled, multi-center, double-masked study to assess the efficacy, safety and tolerability of a single subretinal injection of AVA-101 in subjects with wet AMD in comparison to current anti-VEGF therapies. The trial will include approximately 120 subjects and have endpoints similar to the Phase 2a trial.

Additional Markets for AVA-101

Beyond wet AMD, there are additional ophthalmic diseases where VEGF is known to play a central role, including DME and macular edema following RVO. Like wet AMD patients, these patients are currently treated with frequent injections into the eye with anti-VEGF agents.

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DME is the leading cause of blindness in young adults in developed countries, affecting 12% and 28% of type 1 and type 2 diabetic patients, respectively, as published in the *World Journal of Diabetes* (2011). There are potentially many factors leading to the development of DME including poor control of diabetes, hypertension and dyslipidemia. These factors result in leakage of intravascular liquid into the interstitial space in the eye. Lucentis is currently approved for treatment of DME and Regeneron has recently filed for FDA approval of EYLEA for DME with the FDA.

There are an estimated 2.5 million patients in the world with RVO. In RVO, a retinal vein, which is responsible for draining blood from the eye, becomes obstructed. Both Lucentis and EYLEA have been approved in the United States, Europe and several other countries as treatments to alleviate symptoms of this disease.

AVA-201 for the Prevention of Wet AMD

According to the CDC, approximately 7.3 million patients in the United States are at high risk of developing wet AMD. Within this group, we believe that we can identify a subset of the patients at the highest risk of progressing to wet AMD through a combination of clinical and genetic factors. We believe these patients represent a highly motivated subgroup who could benefit from AVA-201 by preventing the progression from intermediate AMD to advanced wet AMD and the associated vision loss.

AVA-201 is our next generation anti-VEGF gene therapy product candidate, which we are developing for the prevention of wet AMD. AVA-201 delivers the same sFLT-1 expressing gene as AVA-101 but uses next-generation AAV vector delivery method. AVA-201 is administered by an intravitreal injection directly into the vitreous, the jelly-like substance inside the eye. Intravitreal injections are commonly performed, and represent a relatively convenient and low-risk procedure. Furthermore, AVA-201 uses an AAV vector that has been specifically selected through our proprietary directed evolution technology to overcome the physical barrier presented by the anatomy of the retina, leading to high rates of transduction of retinal cells. Based on the features of AVA-201, we are positioning this product candidate for prophylaxis use in patients with earlier forms of AMD. We expect to begin IND-enabling studies in 2015. We own exclusive rights for the development and commercialization of AVA-201 worldwide.

AVA-201 Preclinical Study

To establish proof of concept for the prevention of wet AMD, we tested whether sFLT-1 could prevent the onset of wet AMD symptoms in a non-human primate model. In this study, published in the journal *Molecular Therapy* (2005), non-human primates were transduced with AAV encoding sFLT-1 in one eye, and a control vector in the other eye. At 16 months, choroidal neovascularization, or growth of new blood vessels in the choroid of the eye, was induced by laser irradiation and assessed at two and four weeks. While 46% of control eyes developed lesions by Week 4, none of the treated eyes developed lesions. Therefore, a single dose of the treatment had prevented disease development 17 months later. This initial study, which used AVA-101 as a proof-of-concept, demonstrated that upregulation of sFLT-1 could effectively prevent development of choroidal neovascularization, a major symptom of wet AMD.

Long-Term Prevention of Choroidal Neovascularization in Non-Human Primates

Lesions Graded on Fundus Fluorescein Angiogram (Leaking / Total)		
Subject	Right Eye (sFLT-1 Treated)	Left Eye (Inactive Protein)
1	0 / 8	6 / 8
2	0 / 8	3 / 8
3	0 / 8	2 / 8

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Future Clinical Development for AVA-201

We intend to initiate IND-enabling studies for AVA-201 in 2015, followed by a Phase 1 clinical trial. If AVA-201 demonstrates efficacy for the prevention of wet AMD, we intend to pursue other indications, such as DME and RVO.

AVA-311 for the Treatment of Juvenile X-linked Retinoschisis

XLRS is an inherited retinal disease that occurs almost exclusively in males. It is caused by mutations in the RS1 gene located on the X chromosome. The RS1 protein binds to the surface of the photoreceptors and bipolar cells in the retina and is crucial in maintaining the tissue's integrity. Disruption in the production of the RS1 protein may cause schisis, or splitting, of the retinal layers or leakage in the blood vessels of the retina. These complications lead to severe vision impairment or blindness and often manifest early in childhood. We believe that approximately 10,000 boys and young men suffer from XLRS.

As part of our Collaboration Agreement with Regeneron, we are conducting studies on AVA-311 for the potential treatment of XLRS, a genetic disease affecting boys and young men with no approved therapy. Regeneron will be responsible for various preclinical studies of AVA-311 conducted as part of our collaboration. AVA-311 is comprised of an optimized AAV vector using our directed evolution technology that intravitreally delivers the RS1 gene in the eye to potentially achieve a functional cure for patients. As part of our collaboration with Regeneron, if it exercises its option it will be responsible for all preclinical studies and clinical trials for AVA-311 and will retain worldwide commercialization rights. We have the option to share up to 35% of the development costs and profits from this product candidate.

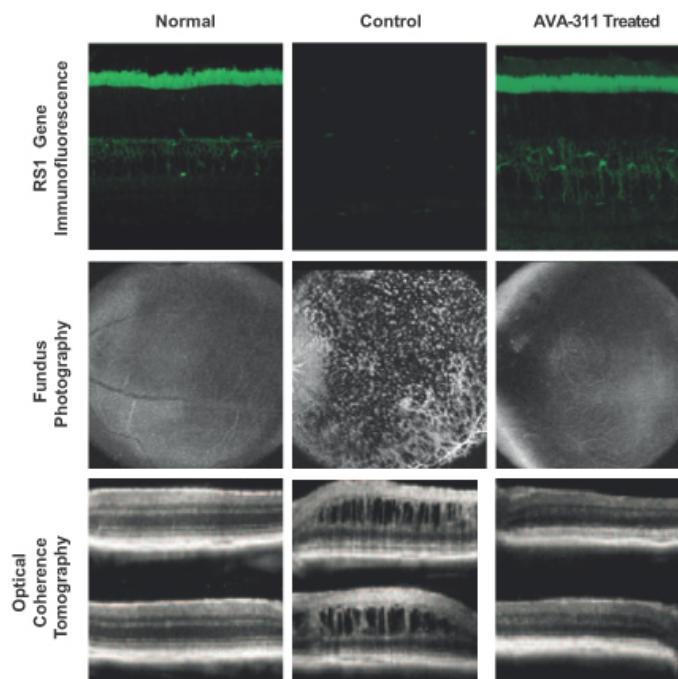
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[Table of Contents](#)**AVA-311 Preclinical Study**

Working with collaborators, we completed a preclinical study with AVA-311 in a mouse model of XLRS that mimics many of the features of the disease by suppressing the RS1 gene in mice. The mice were given a single intravitreal injection of AVA-311 in one eye, and the other eye was left untreated. Mice were monitored for four months. As shown in the immunofluorescence images in Row 1 below, treated eyes exhibited high levels of RS1 protein expression, localized in photoreceptor outer segments of the retina, at levels that are comparable to those found in normal eyes. In addition, as shown in Row 2 by the fundus photographs of the retina and in Row 3 by cross-section images based on optical coherence tomography, AVA-311 restored the appearance of a normal retina.



To evaluate retinal function, electroretinography (ERG), which measures the electrical responses of various cell types in the retina, was used in the preclinical study of AVA-311. Treated eyes exhibited significant improvement in function after one month, and this improvement was maintained over four months. Conversely, retinal function in untreated eyes was lower and continued to decline over this four-month period.

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Future Opportunities

In addition to AVA-101, AVA-201 and AVA-311, we are using our Ocular BioFactory platform to develop other undisclosed product candidates. These product candidates are focused on treating prevalent and rare ophthalmic diseases where a single administration of our therapy can potentially provide a functional cure. Some of these future opportunities are highlighted in the table below.

Major Diseases	Rare Diseases	
Glaucoma	Retinitis Pigmentosa	Leber's Congenital Amaurosis
Geographic Atrophy	Choroideremia	Macular Telangiectasia
Diabetic Retinopathy		

Manufacturing

We produce our AAVs using a proprietary manufacturing process based on insect cells and baculoviruses, a common family of viruses found in invertebrates. This approach is well suited for the production of large quantities of AAVs, as it takes advantage of efficiency of viral infection coupled with the high density and scalability of insect cells grown in serum-free suspension cultures. Compared to the mammalian cell-based approaches commonly used in the field, our manufacturing process is designed to produce higher yields of vectors in a cost-effective manner.

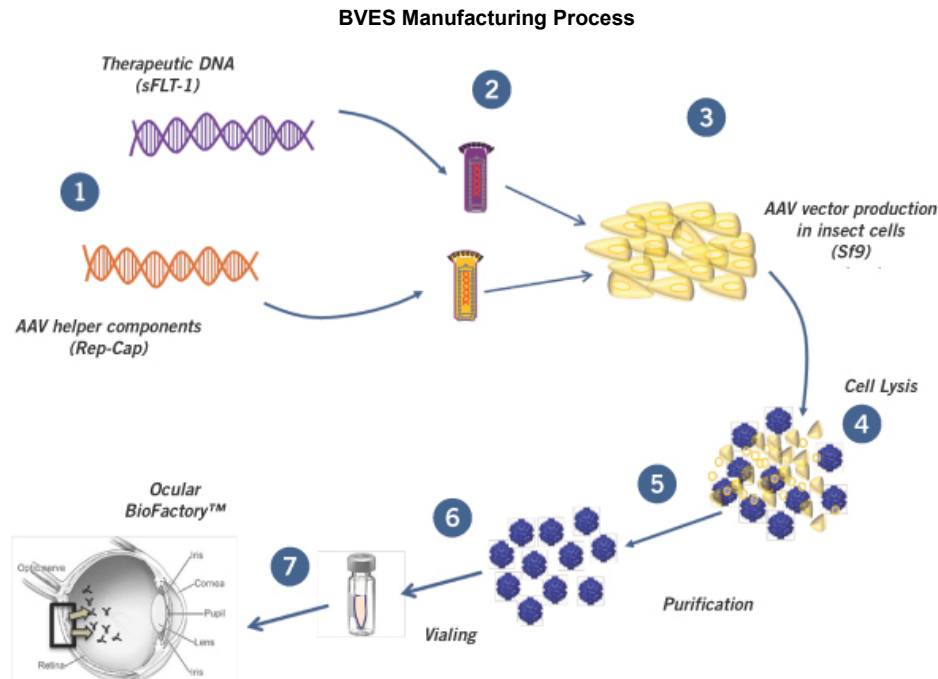
Our BVES manufacturing process is presented in the figure below.

- 1) The process begins with two DNA constructs, one encoding the therapeutic protein and the other encoding AAV helper components encoding the AAV capsid and for replication of vectors.
- 2) Each DNA construct is inserted into the genome of a baculovirus to create two types of recombinant baculoviruses.
- 3) The two baculoviruses are used to transduce insect cells, which in turn produce large amounts of AAV vectors containing the therapeutic gene of interest.
- 4) The transduced cells are then harvested and treated with a lysis buffer solution to burst the insect cells and release the AAV vectors.
- 5) AAV vectors are then purified to remove unwanted debris.
- 6) Following purification, the vectors are formulated in a physiological solution and placed in vials.
- 7) The resulting drug product is then used to create an Ocular BioFactory for the treatment of ophthalmic diseases.

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We have entered into a manufacturing technology license agreement pursuant to which we and Lonza Houston, Inc. are assessing certain technology potentially useful for the manufacture of our products. The license agreement provides that the parties will conduct activities to evaluate such technology and that the Company may elect to engage Lonza to manufacture our products. We also granted to Lonza certain licenses to practice the manufacturing technology for products other than those being developed by us, our affiliates or sublicensees.

Competition

The biopharmaceutical industry is characterized by intense and dynamic competition to develop new technologies and proprietary therapies. Any product candidates that we successfully develop and commercialize will have to compete with existing therapies and new therapies that may become available in the future. While we believe that our Ocular BioFactory platform, differentiated product candidates and scientific expertise in the field of gene therapy provide us with competitive advantages, we face potential competition from various sources, including larger and better-funded pharmaceutical, specialty pharmaceutical and biotechnology companies, as well as from academic institutions, governmental agencies and public and private research institutions.

AVA-101 will compete with a variety of therapies currently marketed and in development for wet AMD using therapeutic modalities such as biologics, small molecules and gene therapy. Existing anti-VEGFs, Lucentis, EYLEA and Avastin, are well established therapies and are widely accepted by physicians, patients and third-party payers as the standard of care for the treatment of wet AMD.

There are several other companies with marketed products or products in development for the treatment of wet AMD, including Allergan, Iconic Therapeutics, Inc., LPath Therapeutics Inc., Novartis, Ocular Therapeutix, Inc., Ophthotech Corporation, Hoffmann-La Roche Ltd., Neurotech Pharmaceuticals, Inc. and Valeant Pharmaceuticals North America LLC.

Our preclinical product candidates are being developed for the treatment of prevalent or rare ophthalmic diseases, such as the prevention of wet AMD and XLR5, for which there are no approved therapies. However, there are

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multiple companies developing gene therapies for ophthalmic diseases, including Applied Genetic Technologies, Asklepios, Eos Neuroscience, GenSight, Genzyme, Hemera Biosciences, ReGenX, RetroSense and Spark Therapeutics.

Many of our competitors, either alone or with their strategic partners, have substantially greater financial, technical and human resources than we do and significantly greater experience in the discovery and development of product candidates, obtaining FDA and other regulatory approvals of treatments and commercializing those treatments. Accordingly, our competitors may be more successful than us in obtaining approval for treatments and achieving widespread market acceptance. Our competitors' treatments may be more effective, or more effectively marketed and sold, than any treatment we may commercialize and may render our treatments obsolete or non-competitive before we can recover the expenses of developing and commercializing any of our treatments.

Mergers and acquisitions in the biotechnology and pharmaceutical industries may result in even more resources being concentrated among a smaller number of our competitors. These competitors also compete with us in recruiting and retaining qualified scientific and management personnel and establishing clinical study sites and subject registration for clinical studies, as well as in acquiring technologies complementary to, or necessary for, our programs. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

We anticipate that we will face intense and increasing competition as new drugs enter the market and advanced technologies become available. We expect any treatments that we develop and commercialize to compete on the basis of, among other things, efficacy, safety, convenience of administration and delivery, price, the level of generic competition and the availability of reimbursement from government and other third-party payers.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, we expect that our therapeutic products, if approved, will be priced at a significant premium over competitive generic products and our ability to compete may be affected in many cases by insurers or other third-party payers seeking to encourage the use of generic products.

License and Collaboration Agreements***Regeneron Research Collaboration and License Agreement***

In May 2014, we entered into the Collaboration Agreement with Regeneron to research, develop and commercialize certain gene therapy products based on our proprietary viral vectors that express transgenes encoding molecules that modulate up to a total of eight specified targets, and encoding certain endogenous molecules known to bind to and modulate such targets. Such products, including AVA-311, are referred to collectively as "Products." Pursuant to the Collaboration Agreement, we and Regeneron will conduct a research program to identify potential Products for a specified time period. Regeneron will bear all costs of performing research under the Collaboration Agreement. Regeneron has a right to substitute a certain number of such targets and may, subject to a payment to us, expand the collaboration beyond the four initially designated targets to include up to four additional targets not currently being researched or developed by Avalanche, and endogenous molecules known to bind to and modulate such additional targets, in the research program. Regeneron has an option, exercisable with respect to all Products containing transgenes expressing molecules that modulate one of the specified targets, to obtain an exclusive, worldwide license to research, develop, use, import, export, make, manufacture and commercialize such Products for the treatment, prevention or diagnosis of human disease or other medical disorders. Regeneron may exercise this option prior to the expiration of the term of the research program, within a certain time period after the acceptance for filing with the FDA of the IND for such Products. Regeneron must pay us an option fee each time it exercises an option.

Regeneron has the right to file an IND with the FDA for Products prior to exercising its option. If Regeneron exercises its option for specified Products, Regeneron will be primarily responsible for developing, obtaining and maintaining regulatory approval for, and commercializing such Products.

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We have a right to co-fund costs of developing, manufacturing and commercializing Products containing transgenes encoding molecules capable of modulating a target with respect to which Regeneron has exercised its option, subject to certain exceptions. We may exercise this co-funding right up to two times. If we exercise such right, we may elect to bear up to 35% of all development costs incurred for such Products. For any co-funded Products, Regeneron's payment obligations extend until the Product is no longer sold in the applicable territory. For those Products for which we exercise this option, either party may opt out of sharing development costs for all Products containing transgenes encoding molecules capable of modulating a protein target, in which case the other party may continue to develop and commercialize such Products, subject to the payment of a royalty to the other party ranging from low-single digit to low double digit royalties. While Regeneron will record all revenue from sales of the co-funded Products, Regeneron will share in the net profits and losses of sales of any Products for which we exercised our co-funding right, with each party receiving a share of profits and bearing its share of losses in accordance with the share of development costs borne by each party for such Product, provided that neither party exercises its opt-out right for such Products.

Additionally, we granted to Regeneron a time-limited right of first negotiation for a potential license to develop and commercialize AVA-101. Such right may be exercised within a specified time period following the first Phase 1 clinical trial for AVA-101. If Regeneron wishes to exercise such right, it must make a payment to us. If Regeneron exercises its right to negotiate and makes such payment, but the parties do not enter into an agreement under which Regeneron obtains such a license, we shall be free to enter into negotiations with third parties provided that for a certain period after expiration of the negotiation period, we may not grant a third party such a license on terms that are less favorable, when taken as a whole, to us than the last proposed offer we made to Regeneron without first offering Regeneron the right to acquire or license AVA-101 on terms and conditions that provide us substantially the same economic value.

Under the Collaboration Agreement, Regeneron made an initial payment of \$8.0 million dollars for collaboration research costs, a one-time option fee and a one-time license grant fee.

In addition to the initial payment, Regeneron may make the following payments to us:

- reimbursement for additional collaboration research costs;
- up to \$80.0 million in development and regulatory milestones for product candidates directed toward each of the eight therapeutic candidates, for a combined total of up to \$640.0 in potential milestone payments for product candidates directed toward all eight therapeutic targets subject to the Collaboration Agreement; and
- tiered, low- to mid-single digit royalties on annual net sales, subject to certain adjustments.

For each Product, Regeneron's payment obligations extend until the last to occur of the following: (i) the discontinuation of development of the Product or (ii) once a Product is approved by the FDA, the later of (x) the duration of patent coverage for the Product or (y) ten years after first commercial sale of the Product in a particular territory.

The Collaboration Agreement continues until the expiration of the option period for all Products, which occurs on May 1, 2017 if Regeneron has not exercised any options for a Product prior to such date. If Regeneron exercises an option for a Product prior to such date, the Collaboration Agreement continues in effect with respect to that Product on a country-by-country basis until the expiration of all payment obligations under the Collaboration Agreement. The Collaboration Agreement may also be terminated (i) by Regeneron at will, either in its entirety or on a target by target basis, upon 30 days' prior written notice to us, (ii) by either party, upon written notice in connection with a material breach remaining uncured 60 days after initial written notice, (iii) by us, if Regeneron challenges the patent rights licensed by us under the Collaboration Agreement or (iv) by either party, for insolvency of the other party.

University of California License Agreement

In May 2010, we entered into a license agreement with Regents as amended in September 2013. Under the license agreement, the Regents have granted to us an exclusive (even as to the Regents) license, with the right to grant sublicenses, under the Regents' undivided interest in patent rights covering a method of using recombinant gene delivery vectors for treating or preventing diseases of the eye, to develop, make, have made, use offer for sale,

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import, export and sell products covered by such patent rights in all fields of use in the United States. The licensed patent rights are jointly owned by the Regents and Chiron Corporation, but our license extends only to the Regents' interest in such patent rights.

Under the license agreement, we are required to diligently proceed with the development, manufacture and sale of licensed products, which includes obligations to meet certain development-stage milestones within specified periods of time, and to market the resulting licensed products in sufficient quantity to meet market demand. We have the right and option to extend the date by which we must meet any milestone by six-months up to two times by paying an extension fee for each such extension.

We have paid the Regents a license fee of \$100,000, and we are required pay the Regents an annual license maintenance fee equal to \$6,000. We are also obligated to make milestone payments totaling up to \$900,000 upon reaching certain stages of development of the licensed products for one indication, and totaling up to \$500,000 for each subsequent indication for which licensed products are developed, for up to a maximum of two additional indications. We must pay the Regents a low single-digit royalty on net sales of the licensed products by us or our sublicensees, subject to a minimum annual royalty payment of \$50,000 beginning in the calendar year after the first commercial sale of a licensed product, until the patent rights upon which such royalties are based expire or are held invalid, which is currently expected to occur in 2020, subject to any potential patent term extensions. We are obligated to reimburse the Regents for expenses associated with the prosecution and maintenance of the licensed patents. Finally, we are obligated to pay the Regents a mid-teen percentage of non-royalty licensing revenue we receive from sublicensees.

Our license agreement with the Regents continues until the expiration of our royalty obligations. We may terminate this agreement without cause at any time upon 30 days' prior written notice to the Regents. The Regents may terminate this agreement for a breach by us that remains uncured for 60 days, if we become insolvent, if we directly or through a third party file a claim that a licensed patent right is invalid or unenforceable or if we fail to meet or extend the date for meeting certain diligence milestones.

Intellectual Property**Overview**

We strive to protect and enhance the proprietary technology, inventions, and improvements that are commercially important to the development of our business, including seeking, maintaining, and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets relating to our proprietary technology platform and on know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in the field of gene therapy that may be important for the development of our business. We additionally may rely on regulatory protection afforded through data exclusivity, market exclusivity and patent term extensions where available.

Our commercial success may depend in part on our ability to obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce our patents; preserve the confidentiality of our trade secrets; and operate without infringing the valid enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing our products may depend on the extent to which we have rights under valid and enforceable licenses, patents or trade secrets that cover these activities. In some cases, these rights may need to be enforced by third party licensors. With respect to both licensed and company-owned intellectual property, we cannot be sure that patents will be granted with respect to any of our pending patent applications or with respect to any patent applications filed by us in the future, nor can we be sure that any of our existing patents or any patents that may be granted to us in the future will be commercially useful in protecting our commercial products and methods of manufacturing the same.

We have 27 pending patent applications in the United States and corresponding foreign patent applications. At least 18 patent applications have been filed in the United States and corresponding foreign jurisdictions by or on behalf of universities which have granted us exclusive license rights to the technology. To date, 12 patents have issued to us or to our licensors. Our policy is to file patent applications to protect technology, inventions and improvements to

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inventions that are commercially important to the development of our business. We seek United States and international patent protection for a variety of technologies, including: research tools and methods, methods for transferring genetic material into cells, AAV-based biological products, methods for treating diseases of interest and methods for manufacturing our AAV-based products. We also intend to seek patent protection or rely upon trade secret rights to protect other technologies that may be used to discover and validate targets and that may be used to identify and develop novel biological products. We seek protection, in part, through confidentiality and proprietary information agreements. We are a party to various other license agreements that give us rights to use specific technologies in our research and development.

Company Owned IP

We own a family of patent applications that are directed to AAV-based compositions and methods for treating or preventing eye diseases associated with neovascularization. The applications in this family relate to the AVA-101 composition, various unit dosages, dosing regimens and routes of administration. Four applications in this family are pending in the United States, and one application is pending in Taiwan. In addition, one application in this family is pending under the Patent Cooperation Treaty (PCT), from which we expect to file various national patent applications outside the United States. Patents that grant from this patent family are generally expected to expire in 2033, subject to possible patent term extensions.

We are also pursuing innovative ways to regulate the expression of transgenes in tissues. To that end, we have, in collaboration with Stanford University, filed a PCT application that is directed to methods for regulating gene expression in a subject. Any patents that grant from this application are expected to expire in 2033, subject to possible patent term extensions.

Licensed IP

We have obtained exclusive licenses to patents directed to both compositions of matter and methods of use.

For example, we have exclusively licensed the rights of the Regents to a U.S. patent directed to methods of treating ocular disease that relate to methods of using AVA-101. This patent is co-owned by the Regents and by Chiron Corporation, and will expire in 2020, unless a term extension is obtained for such patent. There are no foreign patents in this patent family.

We also have obtained an exclusive license to a U.S. patent having composition of matter claims directed to expression vectors that encode a soluble VEGF inhibitor. This patent is expected to expire in 2015. There are no foreign patents in this patent family.

We have exclusively licensed several families of patents and applications that relate to variant rAAV virions having desirable characteristics, such as increased infectivity, as well as novel methods to screen for such variants.

One patent family that we have exclusively licensed includes granted patents in Australia, Germany, France, the United Kingdom and Spain; two pending U.S. patent applications; and a pending patent application in Canada. The patents are projected to expire in 2024, subject to possible patent term extensions, as are any patents that granted from the pending applications.

Another patent family that we have exclusively licensed includes a granted U.S. patent that is projected to expire in 2031 and a pending U.S. patent application which, if granted, is also projected to expire in 2031, in both cases subject to possible patent term extensions.

We have also nonexclusively licensed rights to a patent family that includes an issued European patent and related Chinese and U.S. patent applications directed to methods of manufacturing. The European patent is expected to expire in 2027, as are any patents that may grant from the related patent applications.

Trademark Protection

We have registered trademarks in for use in connection with our biological products. We may pursue additional registrations for future products in markets of interest.

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In addition to the above, we have established expertise and development capabilities focused in the areas of preclinical research and development, manufacturing and manufacturing process scale-up, quality control, quality assurance, regulatory affairs and clinical trial design and implementation. We believe that our focus and expertise will help us develop products based on our proprietary intellectual property.

Trade Secret Protection

Finally, we may rely, in some circumstances, on trade secrets to protect our technology. We seek to protect our proprietary technology and processes, in part, by entering into confidentiality agreements with our employees, consultants, scientific advisors and contractors. We also seek to preserve the integrity and confidentiality of our data and trade secrets by maintaining physical security of our premises and physical and electronic security of our information technology systems. While we have confidence in these individuals, organizations and systems, agreements or security measures may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our consultants, contractors or collaborators use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Government Regulation

The FDA and comparable regulatory authorities in state and local jurisdictions and in other countries impose substantial and burdensome requirements upon companies involved in the clinical development, manufacture, marketing and distribution of our product candidates. These agencies and other federal, state and local entities regulate research and development activities and the testing, manufacture, quality control, safety, effectiveness, labeling, storage, record keeping, approval, advertising and promotion, distribution, post-approval monitoring and reporting, sampling, and export and import of our product candidates.

In the United States, the FDA regulates drug and biologic products under the Federal Food, Drug, and Cosmetic Act (FDCA), and the FDA's implementing regulations and other laws, including, in the case of biologics, the Public Health Service Act. If we fail to comply with applicable FDA or other requirements at any time during the product development process, clinical testing, the approval process or after approval, we may become subject to administrative or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, license suspension or revocation, withdrawal of an approval, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties or criminal prosecution. Any FDA enforcement action could have a material adverse effect on us. Our product candidates may be subject to regulation by the FDA as biologics. Biologics require the submission of a BLA and approval by the FDA before being marketed in the United States. Similarly, FDA approval is required before any new unapproved drug or dosage form, including a new use of a previously approved drug, can be marketed in the United States.

The process required by the FDA before our product candidates may be marketed in the United States generally involves:

- completion of extensive preclinical laboratory tests, preclinical animal studies and formulation studies all performed in accordance with the FDA's current Good Laboratory Practice regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials in the United States may begin;
- approval by an independent IRB at each clinical trial site before each trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate for each proposed indication;
- prior to commercialization satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP regulations;
- submission to the FDA of a BLA or a new drug application (NDA);
- satisfactory completion of a potential review by an FDA advisory committee, if applicable; and
- FDA review and approval of the BLA or NDA prior to any commercial marketing, sale or shipment of the product.

The pre-clinical and clinical testing and approval process requires substantial time, effort and financial resources, and we cannot be certain that any approvals for our product candidates will be granted on a timely basis, if at all.

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Once a product candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluation of product chemistry, formulation, stability and toxicity, as well as animal studies to assess the characteristics and potential safety and efficacy of the product. The results of pre-clinical tests, together with manufacturing information, analytical data and a proposed clinical trial protocol and other information, are submitted as part of an IND to the FDA. Some pre-clinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, raises concerns or questions relating to one or more proposed clinical trials and places the clinical trial on a clinical hold, including concerns that human research subjects will be exposed to unreasonable health risks. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. As a result, our submission of an IND may not result in FDA authorization to commence a clinical trial. A separate submission to an existing IND must also be made for each successive clinical trial conducted during product development, and the FDA must grant permission, either explicitly or implicitly by not objecting before each clinical trial can begin.

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of qualified investigators. Clinical trials are conducted under protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be used. Each protocol must be submitted to the FDA as part of the IND. An IRB for each medical center proposing to conduct a clinical trial must also review and approve a plan for any clinical trial before it can begin at that center and the IRB must monitor the clinical trial until it is completed. The FDA, the IRB or the sponsor may suspend or discontinue a clinical trial at any time on various grounds, including a finding that the subjects are being exposed to an unacceptable health risk. Clinical testing also must satisfy extensive Good Clinical Practice (GCP) requirements, including the requirements for informed consent.

All clinical research performed in the United States in support of a BLA or an NDA must be authorized in advance by the FDA under the IND regulations and procedures described above. However, a sponsor who wishes to conduct a clinical trial outside the United States may, but need not, obtain FDA authorization to conduct the clinical trial under an IND. If a foreign clinical trial is not conducted under an IND, the sponsor may submit data from the clinical trial to the FDA in support of a BLA or an NDA so long as the clinical trial is conducted in compliance with an international guideline for the ethical conduct of clinical research known as the Declaration of Helsinki and/or the laws and regulations of the country or countries in which the clinical trial is performed, whichever provides the greater protection to the participants in the clinical trial.

Clinical Trials

For purposes of BLA or NDA submission and approval, clinical trials are typically conducted in three or four sequential phases, which may overlap or be combined.

- Phase 1: Clinical trials are initially conducted in a limited population of subjects to test the product candidate for safety, dose tolerance, absorption, metabolism, distribution and excretion in healthy humans or, on occasion, in patients with severe problems or life-threatening diseases to gain an early indication of its effectiveness.
- Phase 2: Clinical trials are generally conducted in a limited subject population to evaluate dosage tolerance and appropriate dosage, identify possible adverse effects and safety risks, and evaluate preliminarily the efficacy of the product candidate for specific targeted indications in subjects with the disease or condition under study.
- Phase 3: Clinical trials are typically conducted when Phase 2 clinical trials demonstrate that a dose range of the product candidate is effective and has an acceptable safety profile. Phase 3 clinical trials are commonly referred to as "pivotal" studies, which typically denotes a study which presents the data that the FDA or other relevant regulatory agency will use to determine whether or not to approve a product candidate. Phase 3 clinical trials are generally undertaken with large numbers of subjects, such as groups of several hundred to several thousand, to further evaluate dosage, to provide substantial evidence of clinical efficacy and to further test for safety in an expanded and diverse subject population at multiple, geographically-dispersed clinical trial sites.
- Phase 4: In some cases, the FDA may condition approval of a BLA or an NDA for a product candidate on the sponsor's agreement to conduct additional clinical trials after the product's approval. In other cases, a

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sponsor may voluntarily conduct additional clinical trials post approval to gain more information about the product. Such post approval trials are typically referred to as Phase 4 clinical trials.

These phases of testing may not be completed successfully within any specified period, if at all. Concurrent with clinical trials, companies usually complete additional animal trials and must also develop additional information about the chemistry and physical characteristics of the product candidate and finalize a process for manufacturing the product candidate in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Biologics License Applications and New Drug Applications

The results of preclinical studies and of the clinical trials, together with other detailed information, including extensive manufacturing information and information on the composition of the product, are submitted to the FDA in the form of a BLA or an NDA requesting approval to market the product for one or more specified indications. The FDA reviews a BLA or an NDA to determine, among other things, whether a product is safe and effective for its intended use.

Once a BLA or an NDA has been accepted for filing, by law the FDA has 180 days to review the application and respond to the applicant. However, the review process is often significantly extended by FDA requests for additional information or clarification. Under the Prescription Drug User Fee Act, the FDA has a goal of responding to BLAs and NDAs within ten months of submission for standard review, but this timeframe is also often extended and FDA review may not occur in a timely basis at all. The FDA may refer the application to an advisory committee for review, evaluation and recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. The FDA may deny approval of a BLA or an NDA if the applicable statutory and regulatory criteria are not satisfied, or it may require additional clinical data or an additional Phase 3 clinical trial. Even if such data are submitted, the FDA may ultimately decide that the BLA or NDA does not satisfy the criteria for approval. Data from clinical trials are not always conclusive and the FDA may interpret data differently than we interpret data. Moreover, even if a product receives approval, the approval may be significantly limited to specific disease and dosages or the indications for use may otherwise be limited, which could restrict the commercial value of the product. Once the FDA approves a BLA or an NDA, or supplement thereto, the FDA may withdraw the approval if ongoing regulatory requirements are not met or if safety problems are identified after the product reaches the market. Where a withdrawal may not be appropriate, the FDA still may seize existing inventory of such product or require a recall of any biologic or drug already on the market. In addition, the FDA may require testing, including Phase IV clinical trials and surveillance programs to monitor the effect of approved biologics or drugs which have been commercialized. The FDA has the authority to prevent or limit further marketing of a biologic or drug based on the results of these post-marketing programs.

Drugs and biologics may be marketed only for the FDA approved indications and in accordance with the provisions of the approved labeling. Further, if there are any modifications to the product, including changes in indications, labeling, or manufacturing processes or facilities, the applicant may be required to submit and obtain FDA approval of a new BLA or BLA supplement or a new NDA or NDA supplement, which may require us to develop additional data or conduct additional preclinical studies and clinical trials.

Before approving an application, the FDA will inspect the facility or the facilities at which the finished biologic or drug product, and sometimes, for drug products, the active drug ingredient, is manufactured, and will not approve the product unless cGMP compliance is satisfactory. The FDA may also inspect the sites at which the clinical trials were conducted to assess their compliance, and will not approve the product unless compliance with GCP requirements is satisfactory.

The testing and approval processes require substantial time, effort and financial resources, and each may take several years to complete. The FDA may not grant approval on a timely basis, or at all. Even if we believe a clinical trial has demonstrated safety and efficacy of one of our product candidates for the treatment of a disease, the results may not be satisfactory to the FDA. Preclinical and clinical data may be interpreted by the FDA in different ways,

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which could delay, limit or prevent regulatory approval. We may encounter difficulties or unanticipated costs in our efforts to secure necessary governmental approvals which could delay or preclude us from marketing drugs. The FDA may limit the indications for use or place other conditions on any approvals that could restrict the commercial application of the biologics or drugs. After approval, certain changes to the approved product, such as adding new indications, manufacturing changes, or additional labeling claims are subject to further FDA review and approval. Depending on the nature of the change proposed, a BLA supplement or an NDA supplement must be filed and approved before the change may be implemented. For many proposed post-approval changes to a BLA or an NDA, the FDA has up to 180 days to review the application. As with new BLAs and NDAs, the review process is often significantly extended by the FDA requests for additional information or clarification.

Other Regulatory Requirements

Any biologics or drugs manufactured or distributed by us or our collaborators pursuant to FDA approvals would be subject to continuing regulation by the FDA, including recordkeeping requirements and reporting of adverse experiences associated with the product. Biologic and drug manufacturers and their subcontractors are required to register their establishments with the FDA and certain state agencies, and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMPs, which impose certain procedural and documentation requirements upon us and our third party manufacturers. Failure to comply with the statutory and regulatory requirements can subject a manufacturer to possible legal or regulatory action, such as warning letters, suspension of manufacturing, seizure of product, injunctive action or possible civil penalties. Adverse event reporting and submission of periodic reports are also required following the FDA approval of a BLA or an NDA. We cannot be certain that we or our present or future third-party manufacturers or suppliers will be able to comply with the cGMP regulations and other ongoing FDA regulatory requirements. If we or our present or future third-party manufacturers or suppliers are not able to comply with these requirements, the FDA may halt our clinical trials, require us to recall a product from distribution or withdraw approval of the BLA for that biologic or the NDA for that drug.

The FDA closely regulates the post-approval marketing and promotion of biologics and drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. A company can make only those claims relating to safety and efficacy that are approved by the FDA. Failure to comply with these requirements can result in adverse publicity, warning letters, corrective advertising and potential civil and criminal penalties. Physicians may prescribe legally available drugs for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. Such off-label uses are common across medical specialties. Physicians may believe that such off-label uses are the best treatment for many patients in varied circumstances. The FDA does not regulate the behavior of physicians in their choice of treatments. The FDA does, however, impose stringent restrictions on manufacturers' communications regarding off-label use.

Other Healthcare Laws and Regulations

If we obtain regulatory approval for any of our product candidates, we may also be subject to healthcare regulation and enforcement by the federal government and the states and foreign governments in which we conduct our business. These laws may impact, among other things, our proposed sales, marketing and education programs. In addition, we may be subject to patient privacy regulation by both the federal government and the states in which we conduct our business. The laws that may affect our ability to operate include, the laws that may affect our ability to operate include:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, receiving, offering or paying remuneration, directly or indirectly, in exchange for or to induce either the referral of an individual for, or the purchase, order or recommendation of, any good or service for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;
- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payers that are false or fraudulent;
- federal criminal laws that prohibit executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters;

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- the federal Physician Payment Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services information related to payments and other transfers of value to physicians, other healthcare providers, and teaching hospitals, and ownership and investment interests held by physicians and other healthcare providers and their immediate family members;
- HIPAA, as amended by HITECH, which governs the conduct of certain electronic healthcare transactions and protects the security and privacy of protected health information; and
- state and foreign law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payer, including commercial insurers; state laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, or otherwise restrict payments that may be made to healthcare providers and other potential referral sources; state laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures; and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and may not have the same effect, thus complicating compliance efforts.

If our operations are found to be in violation of any of the laws described above or any other governmental laws and regulations that apply to us, we may be subject to penalties, including civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment, any of which could adversely affect our ability to operate our business and impact our financial results.

Coverage and Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of any products for which we obtain regulatory approval. In the United States and markets in other countries, sales of any products for which we receive regulatory approval for commercial sale will depend in part on the availability of coverage and reimbursement from third-party payers. Third-party payers include government authorities, managed care providers, private health insurers and other organizations. The process for determining whether a payer will provide coverage for a drug product may be separate from the process for setting the reimbursement rate that the payer will pay for the drug product. Third-party payers may limit coverage to specific drug products on an approved list, or formulary, which might not include all of the FDA-approved drugs for a particular indication. Moreover, a payer's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Adequate third-party reimbursement may not be available to enable us to maintain price levels sufficient to realize an appropriate return on our investment in product development.

Third-party payers are increasingly challenging the price and examining the medical necessity and cost-effectiveness of medical products and services, in addition to their safety and efficacy. In order to obtain coverage and reimbursement for any product that might be approved for sale, we may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain regulatory approvals. Our product candidates may not be considered medically necessary or cost-effective. If third-party payers do not consider a product to be cost-effective compared to other available therapies, they may not cover the product after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow a company to sell its products at a profit. The United States government, state legislatures and foreign governments have shown significant interest in implementing cost containment programs to limit the growth of government-paid health care costs, including price controls, restrictions on reimbursement and requirements for substitution of generic products for branded prescription drugs. By way of example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively, the Affordable Care Act, contains provisions that may reduce the profitability of drug products, including, for example, increased the minimum rebates owed by manufacturers under the Medicaid Drug Rebate Program, extended the rebate program to individuals enrolled in Medicaid managed care plans, addressed a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected, and annual fees based on pharmaceutical companies' share of sales to federal health care programs. Adoption of government controls and measures, and

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tightening of restrictive policies in jurisdictions with existing controls and measures, could limit payments for pharmaceuticals.

The marketability of any products for which we receive regulatory approval for commercial sale may suffer if the government and third-party payers fail to provide adequate coverage and reimbursement. In addition, an increasing emphasis on cost containment measures in the United States and other countries has increased and we expect will continue to increase the pressure on pharmaceutical pricing. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

International Regulation

In addition to regulations in the United States, we or our collaborators will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our future drugs. Whether or not we obtain FDA approval for a drug, we or our collaborators must obtain approval of a drug by the comparable regulatory authorities of foreign countries before commencing clinical trials or marketing of the drug in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, marketing authorizations may be submitted either under a centralized, decentralized or mutual recognition procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure includes selecting one reference member state (RMS), and submitting to more than one member state at the same time. The RMS National Competing Authority conducts a detailed review and prepares an assessment report, to which concerned member states provide comment. The mutual recognition procedure provides for mutual recognition of national approval decisions. Under this procedure, the holder of a national marketing authorization may submit an application to the remaining member states post-initial approval. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

In addition to regulations in Europe and the United States, we or our collaborators will be subject to a variety of foreign regulations governing clinical trials and commercial distribution of our future drugs.

Environmental Regulation

We are subject to numerous foreign, federal, state, and local environmental, health and safety laws and regulations relating to, among other matters, safe working conditions, product stewardship and end-of-life handling or disposition of products, and environmental protection, including those governing the generation, storage, handling, use, transportation and disposal of hazardous or potentially hazardous materials. Some of these laws and regulations require us to obtain licenses or permits to conduct our operations. Environmental laws and regulations are complex, change frequently and have tended to become more stringent over time. Although the costs to comply with applicable laws and regulations, including requirements in the European Union relating to the restriction of use of hazardous substances in products, have not been material, we cannot predict the impact on our business of new or amended laws or regulations or any changes in the way existing and future laws and regulations are interpreted or enforced, nor can we ensure we will be able to obtain or maintain any required licenses or permits.

Employees

As of March 31, 2014, we had 14 full-time employees, including a total of eight employees with M.D. or Ph.D. degrees. Within our workforce, 11 employees are engaged in research and development and three in business development, finance, legal, human resources, facilities, information technology and general management and administration. None of our employees are represented by labor unions or covered by collective bargaining agreements.

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Facilities

Our corporate headquarters are located in Menlo Park, California, where we lease and occupy approximately 10,200 square feet of office space. The current term of our lease expires on May 8, 2020, with an option to extend the term through May 8, 2024.

We believe that our existing facilities are adequate for our current needs. When our lease expires, we may exercise our renewal option or look for additional or alternate space for our operations and we believe that suitable additional or alternative space will be available in the future on commercially reasonable terms.

Legal Proceedings

We are not currently a party to any material legal proceedings.

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MANAGEMENT

Executive Officers and Directors

The following table sets forth information regarding our executive officers and directors, as of March 31, 2014:

NAME	AGE	POSITION(S)
Executive Officers		
Thomas W. Chalberg, Jr., Ph.D.	36	President, Chief Executive Officer and Director
Linda C. Bain	43	Chief Financial Officer
Samuel B. Barone, M.D. ⁽¹⁾	40	Chief Medical Officer
Hans P. Hull	39	Senior Vice President, Legal and Corporate Development
Mehdi Gasmi, Ph.D.	47	Vice President, Pharmaceutical Development
Non-Employee Directors		
Mark S. Blumenkranz, M.D. ⁽²⁾⁽³⁾⁽⁴⁾	63	Chairman of the Board
John P. McLaughlin ⁽²⁾⁽³⁾⁽⁴⁾	62	Director
Steven D. Schwartz, M.D. ⁽³⁾⁽⁴⁾	52	Director
Paul D. Wachter ⁽²⁾	57	Director

⁽¹⁾ Dr. Barone was appointed subsequent to March 31, 2014.

⁽²⁾ Member of the audit committee.

⁽³⁾ Member of the compensation committee.

⁽⁴⁾ Member of the nominating and corporate governance committee.

Executive Officers

Thomas W. Chalberg, Jr., Ph.D. Dr. Chalberg is a co-founder of Avalanche and has been a member of our board of directors since July 2006. He has also served as our President and Chief Executive Officer since October 2010. Prior to joining Avalanche, from December 2005 to October 2010, Dr. Chalberg worked at Genentech, a publicly-traded biotechnology company, where he held a number of roles in ophthalmology and oncology, including Market Development Senior Manager for Lucentis and Avastin, Group Manager leading the Lucentis strategy team and Global Business Lead for Lucentis. From September 2001 to December 2005, Dr. Chalberg was a Howard Hughes Medical Institute Fellow at Stanford University, where his research focused on retinal diseases and new technologies for gene therapy. Dr. Chalberg is currently a member of the Board of Visionary Scientists for Hope for Vision, a non-profit charity supporting vision research. Dr. Chalberg holds an A.B. in Biochemical Sciences from Harvard University, a Ph.D. in Genetics from the Stanford University School of Medicine and an M.B.A. from the Haas School of Business at the University of California, Berkeley. Dr. Chalberg has been chosen to serve on our board of directors due to his role as our President and Chief Executive Officer, as well as his many years of experience in ophthalmology research and development and commercialization.

Linda C. Bain. Ms. Bain has served as our Chief Financial Officer and Treasurer since April 2014. Previously, she served at bluebird bio, a gene therapy biotechnology company, as Chief Accounting Officer and Vice President of Finance and Business Operations from October 2011 to March 2014, and as Treasurer from June 2013 to March 2014. From September 2008 to September 2011, Ms. Bain served as Vice President of Finance at Genzyme Corporation, a biotechnology company. From September 2007 to September 2008, she served as Vice President at Fidelity Investments, and from May 2000 to September 2007, she held a number of positions at AstraZeneca plc, a publicly-traded pharmaceutical company. She received her B.S. in Accounting and Business Administration and an Honors Degree in Accounting and Business Administration from the University of the Free State in South Africa. Ms. Bain is a Certified Public Accountant.

Samuel B. Barone, M.D. Dr. Barone has served as our Chief Medical Officer since June 2014. Previously, from October 2009 until June 2014, Dr. Barone served as a Medical Officer in the Office of Cellular, Tissue and Gene Therapies at the FDA. From October 2010 to June 2014, Dr. Barone also practiced ophthalmology as part of Retina Associates P.C., an eye-care provider. Prior to working at the FDA, between July and October 2009, Dr. Barone

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served as a staff physician practicing ophthalmology at the VA Medical Center in San Diego (part of the VA San Diego Healthcare System). Prior to that, Dr. Barone had a residency in ophthalmology at The New York Eye and Ear Infirmary, as well as a medical and surgical retina fellowship at the University of California, San Diego. Previously, Dr. Barone served on active duty as a flight surgeon for the United States Air Force service members at Andrews Air Force Base and at bases in Korea, Afghanistan and Iraq. He also performed ophthalmology consulting services for Ophthalmology Consultants, P.C., an ophthalmology consultancy, in October 2013 and January 2014. Dr. Barone received his B.S. in Biology from Boston College and his M.D. from The Pennsylvania State University College of Medicine.

Mehdi Gasmi, Ph.D. Dr. Gasmi has served as our Vice President, Pharmaceutical Development since November 2013, and leads manufacturing and quality control efforts for our gene therapy product candidates. From December 2011 to November 2013, as principal of ClinVec Solutions, LLC, Dr. Gasmi provided AAV and lentiviral gene therapy consulting services to various companies, including to Avalanche between June 2013 to October 2013. Prior to that, Dr. Gasmi oversaw production of clinical batches of recombinant AAV and lentiviral gene therapy products for both Génethon, a gene therapy company, where he served as Vice President of Biomanufacturing from July 2009 to December 2011, and for Ceregene, a gene therapy company, where Dr. Gasmi served as Senior Director, Product Development from December 2001 to June 2009. Dr. Gasmi obtained his M.S. and his Ph.D. in Biochemistry from the Claude Bernard University in Lyon, France. He is a member of the American Society of Gene and Cell Therapy.

Hans P. Hull. Mr. Hull has served as our Senior Vice President, Legal and Corporate Development, since July 2014. Previously, he served as our Vice President, Legal and Corporate Development from February 2012 to July 2014. From March 2005 to April 2008, he served as General Manager and then Chief Executive Officer of Orthobond Corporation, a medical device company. From May 2008 to December 2011, he served as a legal and business development consultant for life sciences companies, including Second Genome, Inc., a biotechnology company, and Aprelia Pharmaceuticals Company, a pharmaceutical company. Mr. Hull began his career in life sciences as a strategy consultant to pharmaceutical and biotechnology companies for ZS Associates, Inc. from September 1997 to April 2000 and also worked as an attorney at Heller Ehrman White & McAuliffe LLP from September 2003 to March 2005. Mr. Hull received a A.B. in Chemistry from Princeton University and a J.D. from Boalt Hall School of Law at the University of California, Berkeley.

Directors

Mark S. Blumenkranz, M.D. Dr. Blumenkranz has served as a member of our board of directors since our inception in July 2006 and is a co-founder of Avalanche. Dr. Blumenkranz is a trained vitreoretinal surgeon and Chairman of the Department of Ophthalmology at the Byers Eye Institute at Stanford University. Prior to that, he served on the faculty of the Bascom Palmer Eye Institute in Miami, Florida. Previously, from October 1985 to August 1992, Dr. Blumenkranz founded and served as Director of the Vitreoretinal Fellowship Program at William Beaumont Hospital in Royal Oak, Michigan. From 2000 to 2004, Dr. Blumenkranz served on the scientific advisory board of Eyetech, a biopharmaceutical company. Dr. Blumenkranz currently serves on the boards of directors of Vantage Surgical Systems Inc., Oculogics, Inc., Presbia Holdings, Digisight Technologies Inc. and Oculieve, Inc., all privately held biotechnology or medical device companies. Dr. Blumenkranz received his A.B. in Biology, his M.M.S. in Biochemical Pharmacology and his M.D. all from Brown University, followed by a residency in ophthalmology at Stanford University. Dr. Blumenkranz has been chosen to serve on our board of directors due to his experience as a director and founder of several biotechnology companies, as well as his significant medical expertise in ophthalmology and biotechnology.

John P. McLaughlin. Mr. McLaughlin has served as a member of our board of directors since February 2014. Mr. McLaughlin has been President and Chief Executive Officer of PDL BioPharma, Inc., a publicly traded biopharmaceutical company, since December 2008, and a director since October 2008. Previously, he was the Chief Executive Officer and a director of Anesiva, Inc., formerly known as Corgentech, Inc., a publicly-traded biopharmaceutical company, from January 2000 to June 2008. From December 1997 to September 1999, Mr. McLaughlin was President of Tularik Inc., a biopharmaceutical company. From September 1987 to December 1997, Mr. McLaughlin held a number of senior management positions at Genentech, a publicly-traded biopharmaceutical company. From 1985 to 1987, Mr. McLaughlin was a partner at a Washington, D.C. law firm specializing in food and drug law. Prior to that, Mr. McLaughlin served as counsel to various subcommittees in the

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U.S. House of Representatives, where he worked on FDA-related laws. Mr. McLaughlin cofounded and served as Chairman of the board of directors of Eyetech, a biopharmaceutical company. He also cofounded and served as a director of PEAK Surgical, Inc., a privately-held medical device company. Mr. McLaughlin has served on the board of directors, audit committee and nominating committee of Seattle Genetics, Inc., a publicly-traded biopharmaceutical company, since June 2007. He has also served on the board of directors of Axogen Inc., a publicly-traded biopharmaceutical company, since October 2012. He received his B.A. in Government from the University of Notre Dame and J.D. from the Catholic University of America. Mr. McLaughlin has been chosen to serve on our board of directors due to his significant experience as an officer and director at biopharmaceutical companies, including publicly-traded companies, as well as his substantial expertise in corporate licensing, legal and regulatory matters relating to healthcare.

Steven D. Schwartz, M.D. Dr. Schwartz has served as a member of our board of directors since September 2010, and is a co-founder of Avalanche. Dr. Schwartz is the Ahmanson Professor of Ophthalmology at the Jules Stein Eye Institute at the University of California, Los Angeles, where he has served as an ophthalmologist and vitreoretinal surgeon since 1994 and as Chief of the Retina Division since 2002. Previously, Dr. Schwartz was a principal investigator in a number of early-stage clinical trials for retinal diseases, including the initial studies for ranibizumab (Lucentis), as well as products in gene and cell therapy. Between 2002 and 2005, Dr. Schwartz held various positions at Eyetech, a biopharmaceutical company. Dr. Schwartz currently serves on the board of directors of the American Society of Retina Specialists. Dr. Schwartz has also served on a number of scientific advisory boards, including for Genentech, a publicly-traded biotechnology company, as well as for ophthalmology technology companies Ophthotech, Optos plc and Optimedica Corporation. Dr. Schwartz received his B.A. in from the University of California, Berkeley and his M.D. from the Keck School of Medicine at the University of Southern California, followed by a Residency in Ophthalmology at the University of California, Los Angeles, and a vitreoretinal fellowship at Moorefield's Eye Hospital in London. Dr. Schwartz has been chosen to serve on our board of directors due to his substantial scientific expertise as an ophthalmologist and medical researcher, as well as his experience at several ophthalmology-focused technology companies.

Paul D. Wachter. Mr. Wachter has served as a member of our board of directors since April 2014. Mr. Wachter has been the Chief Executive Officer of Main Street Advisors, which he also founded, since 1997. Prior to forming Main Street Advisors, from June 1993 to March 1997, Mr. Wachter was Managing Director of Schroder & Co. Incorporated, an asset management company. From December 1991 to June 1993, Mr. Wachter was a managing director at Kidder, Peabody & Co., an investment banking firm. Since October 2010, Mr. Wachter has served on the board of directors and audit committee of Time Warner, Inc., a publicly-traded media company, and he also currently serves on the boards of directors of several private media companies, including Beats Electronics LLC and Haworth Marketing + Media. Mr. Wachter received his B.S. in Business Administration from the Wharton School of the University of Pennsylvania and his J.D. from the Columbia University School of Law. Mr. Wachter is a member of the New York State Bar and a Series 7 licensed stockbroker. Mr. Wachter has been chosen to serve on our board of directors due to his substantial expertise in business, financial and corporate governance matters.

Board Composition

In accordance with our amended and restated certificate of incorporation which will become effective upon the closing of this offering, our board of directors will be divided into three classes with staggered three-year terms. At each annual meeting of stockholders, the successors to directors whose terms then expire will be elected to serve from the time of election and qualification until the third annual meeting following their election. After the consummation of this offering, our directors will be divided among the three classes as follows:

- the Class I directors will be Thomas W. Chalberg, Jr., Ph.D. and Paul D. Wachter, and their terms will expire at the annual meeting of stockholders to be held in 2015;
- the Class II directors will be Steven D. Schwartz, M.D. and John P. McLaughlin, and their terms will expire at the annual meeting of stockholders to be held in 2016; and
- the Class III director will be Mark S. Blumenkranz, M.D., and his term will expire at the annual meeting of stockholders to be held in 2017.

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Our amended and restated certificate of incorporation will provide that the number of directors may be changed only by resolution of the board of directors. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of one-third of the directors. The division of our board of directors into three classes with staggered three-year terms may delay or prevent a change of our management or a change of control at our company.

Leadership Structure of the Board

Our bylaws and corporate governance guidelines provide our board of directors with flexibility to combine or separate the positions of Chairman of the board of directors and Chief Executive Officer and/or the implementation of a lead director in accordance with its determination that utilizing one or the other structure would be in the best interests of our company. Dr. Blumenkranz currently serves as the Chairman of our board of directors. All of our directors are encouraged to make suggestions for board of directors agenda items of pre-meeting materials. Additionally, in his role as Chairman of the board, Dr. Blumenkranz presides over the executive sessions of the board of directors in which Dr. Chalberg does not participate and serve as a liaison to Dr. Chalberg and management on behalf of the independent members of the board of directors.

Our board of directors has concluded that our current leadership structure is appropriate at this time. However, our board of directors will continue to periodically review our leadership structure and may make such changes in the future as it deems appropriate.

Director Independence

Upon the consummation of this offering, our common stock will be listed on The NASDAQ Global Market. Rule 5605 of the NASDAQ Marketplace Rules (NASDAQ Listing Rules) requires that independent directors compose a majority of a listed company's board of directors within one year of listing. In addition, the NASDAQ Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation, and nominating and corporate governance committees be independent and that audit committee members also satisfy independence criteria set forth in Rule 10A-3 under the Exchange Act. Under NASDAQ Listing Rule 5605(a)(2), a director will only qualify as an "independent director" if, in the opinion of our board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3 under the Exchange Act, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee: (1) accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries; or (2) be an affiliated person of the listed company or any of its subsidiaries. In addition to satisfying general independence requirements under the NASDAQ Listing Rules, members of the compensation committee must also satisfy additional independence requirements set forth in NASDAQ Listing Rule 5605(d)(2). In order to be considered independent for purposes of NASDAQ Listing Rule 5605(d)(2), a member of a compensation committee of a listed company may not, other than in his or her capacity as a member of the compensation committee, the board of directors, or any other board committee, accept, directly or indirectly any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries. Additionally, the board of directors of the listed company must consider whether the compensation committee member is an affiliated person of the listed company or any of its subsidiaries and if so, must determine whether such affiliation would impair the director's judgment as a member of the compensation committee.

In July 2014, our board of directors undertook a review of its composition, the composition of its committees and the independence of each director. Based upon information requested from and provided by each director concerning his background, employment and affiliations, including family relationships, our board of directors has determined that none of Drs. Blumenkranz and Schwartz and Messrs. McLaughlin and Wachter, representing four of five directors, has a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director and that each of these directors is "independent" as that term is defined under NASDAQ rules. Our board of directors also determined that Dr. Blumenkranz and Messrs. McLaughlin and Wachter, who are members of our audit committee, Drs. Blumenkranz and Schwartz, and Mr. McLaughlin, who comprise our compensation committee, and Drs. Blumenkranz and Schwartz and Mr. McLaughlin, who comprise our nominating and governance committee, satisfy the independence standards for those committees established by applicable SEC rules and NASDAQ rules.

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Upon completion of this offering, our nominating and corporate governance committee will be responsible for reviewing with the board of directors, on an annual basis, the appropriate characteristics, skills and experience required for the board of directors as a whole and its individual members. In evaluating the suitability of individuals candidates (both new candidates and current members), the nominating and corporate governance committee, in recommending candidates for election, and the board of directors, in approving (and, in the case of vacancies, appointing) such candidates, will take into account many factors, including the following:

- diversity of personal and professional background, perspective and experience;
- personal and professional integrity, ethics and values;
- experience in corporate management, operations or finance, such as serving as an officer or former officer of a publicly held company, and a general understanding of marketing, finance and other elements relevant to the success of a publicly-traded company in today's business environment;
- experience relevant to our industry and with relevant social policy concerns;
- experience as a board member or executive officer of another publicly held company;
- relevant academic expertise or other proficiency in an area of our operations;
- practical and mature business judgment, including ability to make independent analytical inquiries;
- promotion of a diversity of business or career experience relevant to our success; and
- any other relevant qualifications, attributes or skills.

Currently, our board of directors evaluates, and following the completion of this offering will evaluate, each individual in the context of the board of directors as a whole, with the objective of assembling a group that can best maximize the success of the business and represent stockholder interests through the exercise of sound judgment using its diversity of experience in these various areas.

Role of Board in Risk Oversight Process

Risk assessment and oversight are an integral part of our governance and management processes. Our board of directors encourages management to promote a culture that incorporates risk management into our corporate strategy and day-to-day business operations. Management discusses strategic and operational risks at regular management meetings, and conducts specific strategic planning and review sessions during the year that include a focused discussion and analysis of the risks facing us. Throughout the year, senior management reviews these risks with the board of directors at regular board meetings as part of management presentations that focus on particular business functions, operations or strategies, and presents the steps taken by management to mitigate or eliminate such risks.

Our board of directors does not have a standing risk management committee, but rather administers this oversight function directly through our board of directors as a whole, as well as through various standing committees of our board of directors that address risks inherent in their respective areas of oversight. In particular, our board of directors is responsible for monitoring and assessing strategic risk exposure, our audit committee is responsible for overseeing our major financial risk exposures and the steps our management has taken to monitor and control these exposures. The audit committee also monitors compliance with legal and regulatory requirements. Our nominating and governance committee monitors the effectiveness of our corporate governance guidelines and considers and approves or disapproves any related persons transactions. Our compensation committee assesses and monitors whether any of our compensation policies and programs has the potential to encourage excessive risk-taking.

Board Committees

Our board of directors has the following standing committees: an audit committee, a compensation committee and a nominating and corporate governance committee. Our board of directors may establish other committees to facilitate the management of our business. The composition and functions of each committee are described below.

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Our audit committee oversees our corporate accounting and financial reporting process. Among other matters, the audit committee:

- appoints our independent registered public accounting firm;
- evaluates the independent registered public accounting firm's qualifications, independence and performance;
- determines the engagement of the independent registered public accounting firm;
- reviews and approves the scope of the annual audit and the audit fee;
- discusses with management and the independent registered public accounting firm the results of the annual audit and the review of our quarterly consolidated financial statements;
- approves the retention of the independent registered public accounting firm to perform any proposed permissible audit and non-audit services;
- monitors the rotation of partners of the independent registered public accounting firm on our engagement team as required by law;
- is responsible for reviewing our consolidated financial statements and our management's discussion and analysis of financial condition and results of operations to be included in our annual and quarterly reports to be filed with the SEC;
- reviews our critical accounting policies and estimates;
- reviews related party transactions; and
- annually reviews the audit committee charter and the audit committee's performance.

The current members of our audit committee are Dr. Blumenkranz and Messrs. McLaughlin and Wachter. Mr. McLaughlin serves as the chairman of the committee. All members of our audit committee meet the requirements for financial literacy under the applicable rules and regulations of the SEC and NASDAQ. Our board of directors has determined that Mr. McLaughlin is an audit committee financial expert as defined under the applicable rules of the SEC and has the requisite financial sophistication as defined under the applicable NASDAQ rules and regulations. Under the rules of the SEC and NASDAQ, members of the audit committee must also meet heightened independence standards. Our board has determined that each of Dr. Blumenkranz, Mr. McLaughlin and Mr. Wachter meet these heightened independence standards. The audit committee operates under a written charter that satisfies the applicable standards of the SEC and NASDAQ.

Compensation Committee

Our compensation committee reviews and recommends policies relating to compensation and benefits of our officers, directors and employees. The compensation committee reviews and approves corporate goals and objectives relevant to compensation of our Chief Executive Officer and other executive officers, evaluates the performance of these officers in light of those goals and objectives, and sets or makes recommendations to the board regarding the compensation of these officers based on such evaluations. The board of directors shall retain the authority to determine and approve, upon the recommendation of the compensation committee, the compensation of the Chief Executive Officer, unless such authority has been delegated to the compensation committee. The compensation committee also approves grants of stock options and other awards under our stock plans. The compensation committee will periodically review and evaluate the performance of the compensation committee and its members, including an annual review of its charter. The current members of our compensation committee are Drs. Blumenkranz and Schwartz and Mr. McLaughlin. Dr. Schwartz serves as the chairman of the committee. Each of the members of our compensation committee is an independent, outside and non-employee director under the applicable rules and regulations of the SEC, NASDAQ and the Code relating to compensation committee independence. The compensation committee operates under a written charter.

Nominating and Corporate Governance Committee

The nominating and corporate governance committee is responsible for making recommendations to our board of directors regarding candidates for directorships and composition and organization of our board of directors. In addition, the nominating and corporate governance committee is responsible for overseeing our corporate governance policies and reporting and making recommendations to our board of directors concerning governance matters. The

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current members of our nominating and corporate governance committee are Drs. Blumenkranz and Schwartz and Mr. McLaughlin. Dr. Blumenkranz serves as the chairman of the committee. Each of the members of our nominating and corporate governance committee is an independent director under the applicable rules and regulations of the SEC and NASDAQ relating to nominating and corporate governance committee independence. The nominating and corporate governance committee operates under a written charter.

There are no family relationships among any of our directors or executive officers.

Compensation Committee Interlocks and Insider Participation

During the fiscal year ended December 31, 2013, or for some portion thereof, Drs. Blumenkranz and Schwartz served as members of the compensation committee. No such person is currently, or has been at any time, one of our officers or employees. None of our executive officers currently serves, or has served during the last completed three fiscal years, as a member of the board of directors or compensation committee of any other entity that has or had one or more executive officers serving as a member of our board of directors or compensation committee.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our employees, officers and directors, including those officers responsible for financial reporting. Following the completion of this offering, the code of business conduct and ethics will be available on our website at www.avalanchebiotech.com. We expect that any amendments to the code, or any waivers of its requirements, will be disclosed on our website.

Limitation on Liability and Indemnification Matters

Our amended and restated certificate of incorporation, which will become effective immediately prior to the consummation of this offering, contains provisions that limit the liability of our directors for monetary damages to the fullest extent permitted by Delaware law. Consequently, our directors will not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duties as directors, except liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemptions as provided in Section 174 of the Delaware General Corporation Law; or
- any transaction from which the director derived an improper personal benefit.

Our amended and restated certificate of incorporation and amended and restated bylaws, which will become effective immediately prior to the consummation of this offering, provide that we are required to indemnify our directors and officers, in each case to the fullest extent permitted by Delaware law. Our amended and restated bylaws also provide that we are obligated to advance expenses incurred by a director or officer in advance of the final disposition of any action or proceeding, and permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in that capacity regardless of whether we would otherwise be permitted to indemnify him or her under Delaware law. We have entered and expect to continue to enter into agreements to indemnify our directors, executive officers and other employees as determined by our board of directors. With specified exceptions, these agreements provide for indemnification for related expenses, including, among other things, attorneys' fees, judgments, fines and settlement amounts incurred by any of these individuals in any action or proceeding. We believe that these bylaw provisions and indemnification agreements are necessary to attract and retain qualified persons as directors and officers. We also maintain directors' and officers' liability insurance.

The limitation of liability and indemnification provisions in our amended and restated certificate of incorporation and amended and restated bylaws may discourage stockholders from bringing a lawsuit against our directors and officers for breach of their fiduciary duty. They may also reduce the likelihood of derivative litigation against our directors and officers, even though an action, if successful, might benefit us and our stockholders. Further, a stockholder's investment may be adversely affected to the extent that we pay the costs of settlement and damages.

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EXECUTIVE AND DIRECTOR COMPENSATION

2013 Summary Compensation Table

The following table sets forth total compensation paid to our named executive officers (NEOs) who are comprised of (1) our principal executive officer and (2) our next two highest compensated executive officers other than the principal executive officer.

NAME AND PRINCIPAL POSITION	YEAR	SALARY (\$)	BONUS (\$) ⁽¹⁾	NON-EQUITY INCENTIVE PLAN COMPENSATION (D)	ALL OTHER COMPENSATION (E)	TOTAL (\$)
Thomas W. Chalberg, Jr., Ph.D. <i>Chief Executive Officer</i>	2013	\$ 297,600	\$ 62,500	\$ —	\$ —	\$360,100
Mehdi Gasmi, Ph.D. ⁽²⁾ <i>Vice President, Pharmaceutical Development</i>	2013	46,500	3,000	—	14,406 ⁽³⁾	63,906
Hans P. Hull <i>Senior Vice President, Legal and Corporate Development</i>	2013	194,674	28,333	—	—	223,007

⁽¹⁾ Bonus represents amounts earned for 2013 performance and paid in 2014.

⁽²⁾ Joined Avalanche on November 1, 2013.

⁽³⁾ Amount represents relocation reimbursement.

Outstanding Equity Awards at 2013 Fiscal Year End

The following table lists all outstanding equity awards held by our NEOs as of December 31, 2013.

NAME	GRANT DATE	OPTION AWARDS			
		NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) EXERCISABLE	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS (#) UNEXERCISABLE	OPTION EXERCISE PRICE (\$)	OPTION EXPIRATION DATE
Thomas W. Chalberg, Jr., Ph.D.	February 24, 2012 ⁽¹⁾	73,333	86,667	0.19	February 23, 2022
	November 15, 2012 ⁽²⁾	281,667	758,333	0.19	November 14, 2022
Mehdi Gasmi, Ph.D. ⁽³⁾	N/A	—	—	—	N/A
Hans P. Hull	February 24, 2012 ⁽⁴⁾	25,208	29,792	0.19	February 23, 2022
	November 15, 2012 ⁽⁵⁾	18,333	36,667	0.19	November 14, 2022

⁽¹⁾ This option vests in equal monthly installments over a period of 48 months measured from February 24, 2012, subject to continuous service upon each such vesting date.

⁽²⁾ This option vests in equal monthly installments over a period of 48 months measured from November 15, 2012, subject to continuous service upon each such vesting date. If the optionee is terminated without "cause" or for "good reason" within 12 months following a change in control, the options will immediately become fully vested.

⁽³⁾ Joined Avalanche on November 1, 2013, but no options were granted in 2013.

⁽⁴⁾ This option vests in equal monthly installments over a period of 48 months measured from February 1, 2012, subject to continuous service upon each such vesting date.

⁽⁵⁾ This option vests in equal monthly installments over a period of 48 months measured from August 1, 2012, subject to continuous service upon each such vesting date. If the optionee is terminated without "cause" or for "good reason" within 12 months following a change in control, the options will immediately become fully vested.

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Table of Contents**Narrative to 2013 Summary Compensation Table and Outstanding Equity Awards at 2013 Fiscal Year End*****Employment Arrangements***

We have entered into offer letter agreements with Dr. Chalberg and Mr. Hull in connection with their employment with us. These agreements provided for "at will" employment and set forth the terms and conditions of employment of each named executive officer, including base salary and annual bonus opportunity. These offer letter agreements each required the execution of our standard proprietary information and invention assignment agreement.

In March 2013, our board of directors set Dr. Chalberg's annual base salary and annual target bonus at \$300,000 and 25% of base salary, respectively, and Mr. Hull's annual base salary and annual target bonus at \$178,500 and 22% of base salary, respectively. Dr. Chalberg's and Mr. Hull's current annual base salaries are \$500,000 and \$300,000, respectively, and current target bonus opportunities are 55% and 30% of base salary, respectively.

Pursuant to Dr. Chalberg's offer letter agreement, in the event he is terminated for any reason other than Cause (as defined below) or resigns for Good Cause (as defined below), he will be entitled to receive severance pay in the amount of six months of salary. The severance provisions of Dr. Chalberg's offer letter have been superseded by the terms of a change in control and severance agreement entered into in connection with this offering.

We entered into an offer letter agreement with Dr. Gasmi in June 2013, pursuant to which Dr. Gasmi commenced employment with us as our Vice President, Pharmaceutical Development in November 2013. The agreement provided for an annual base salary of \$260,000 and eligibility to earn an annual performance bonus, which bonus will be prorated for any year in which he is not employed during the whole calendar year. Dr. Gasmi's target bonus opportunity is currently 25% of base salary. Pursuant to the agreement, on March 5, 2014, we also granted to Dr. Gasmi an option to purchase 110,000 shares of our common stock under our 2006 Equity Incentive Plan. 25% shares underlying the option will vest on the first anniversary of the grant date and the remaining shares will vest in equal monthly installments over the 36 months thereafter.

In addition, the agreement provided for executive relocation assistance, up to \$23,000. In the event that Dr. Gasmi terminates his employment prior to 24 months, he will be obligated to repay all or some of the cash value of the relocation assistance.

We granted each of Drs. Chalberg and Gasmi and Mr. Hull an option to purchase 80,000, 70,000 and 75,000 shares of our common stock, respectively, effective on the date of this offering and having a per share exercise price equal to the per share initial public offering price set forth on the cover of this prospectus. Each option vests over four years from the date of grant, subject to the executive's continued service to our company.

Terms and Conditions of Annual Bonuses

While we do not have a formal bonus program, our board of directors may award discretionary bonuses to incentivize new employees or reward outstanding performance and continued dedication of our current employees.

Change in Control Benefit Plan

Drs. Chalberg and Gasmi and Mr. Hull are also participants in the company's Change in Control Benefit Plan. Under the Change in Control Benefit Plan, in the event that the Company terminates a participant's employment or service without Cause (as defined below) (and other than as a result of death or disability), or if the participant resigns his or her employment or service for Good Reason (as defined below) in either case at any time during the period commencing on a change in control and ending 12 months following the change in control, then 100% of the unvested shares subject to the participant's equity awards issued under the company's 2006 Incentive Equity Plan shall vest and, as applicable, become exercisable immediately prior to the date of such termination.

In July 2014, our compensation committee approved change in control and severance agreements with each of Drs. Chalberg and Gasmi and Mr. Hull. The change in control and severance agreements supersede the Change in Control Plan. Under the agreements, in the event a named executive officer is terminated by us without Cause more than three months prior to a change in control or more than twelve months after a change in control, then he is entitled to a fixed number of months of base salary and continued healthcare coverage and, in the case of Dr. Chalberg, the vesting of outstanding equity awards will immediately accelerate with respect to that number of shares that otherwise would have vested had he remained employed by us for an additional six months. The fixed number of months for Dr. Chalberg is 12 months and for Dr. Gasmi and Mr. Hull is nine months.

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In the event that the named executive officer is terminated by us without Cause or resigns for Good Reason, in each case, within the period commencing three months prior to a change in control and ending on the first anniversary of the change in control, then he is entitled to a fixed number of months of base salary and continued healthcare coverage, a pro-rated bonus for the year of termination and the accelerated vesting of all outstanding equity awards. The fixed number of months for Dr. Chalberg is 18 months and for Dr. Gasmi and Mr. Hull is 12 months.

For the purposes of the Change in Control Plan and the change in control and severance agreements, "Cause" generally means misconduct, including: (i) conviction of any felony or any crime involving moral turpitude or dishonesty; (ii) willful and material breach of the executive's duties that has not been cured within 30 days after written notice from the board of directors; (iii) intentional and material damage to the company's property; or (iv) material breach of the Proprietary Information and Inventions Agreement executed by the executive.

"Good Reason" means any of the following actions taken without Cause by the company or a successor corporation or entity without the participant's consent: (i) substantial reduction of the participant's rate of compensation; (ii) material reduction in the participant's duties, provided, however, that a change in job position (including a change in title) shall not be deemed a "material reduction" unless the participant's new duties are substantially reduced from the prior duties; (iii) failure or refusal of a successor to the company to assume the company's obligations under the plan in the event of certain transactions; (iv) relocation of the participant's principal place of employment or service to a place greater than 50 miles from the participant's then current principal place of employment or service; (v) the requirement to increase the amount of time per week that the participant provides services to the company or (vi) the requirement that the participant cease other employment or consulting engagements, unless such employment and/or consulting engagement results in a direct conflict with the company's business.

Director Compensation

The following table presents the total compensation for each person who served as a non-employee member of our board of directors during the year ended December 31, 2013. Other than as set forth in the table and described more fully below, in 2013 we did not pay any compensation, reimburse any expense of, make any equity awards or non-equity awards to, or pay any other compensation to any of the other non-employee members of our board of directors.

NAME	FEES EARNED OR PAID IN CASH (\$)	STOCK AWARDS (\$)	OPTION AWARDS (\$)	ALL OTHER COMPENSATION (\$)	TOTAL
Mark S. Blumenkranz, M.D.	—	—	—	—	\$ —
Steven D. Schwartz, M.D.	—	—	—	—	\$ —

Non-Employee Director Compensation

Our non-employee directors receive an option to purchase shares of our common stock upon his or her initial election or appointment to our board of directors. Historically, these options have vested in substantially equal monthly installments over the four-year period following the grant date, subject to continued service, and the number of shares of our common stock subject to the options have varied from director to director. In 2014, Mr. McLaughlin and Mr. Wachter were each granted stock options exercisable for 75,000 shares of our common stock, for an aggregate of 150,000 shares. We also reimburse our non-employee directors for travel and other necessary business expenses incurred in the performance of their services for us.

Following the effectiveness of this offering, each member of our board of directors who is not our employee will receive the following cash compensation for board services, as applicable:

- \$40,000 per year for service as a board of directors member;
- \$35,000 per year for service as the independent chairman of the board of directors;
- \$20,000 per year for service as chairman of the Audit Committee;
- \$15,000 per year for service as chairman of the Compensation Committee;
- \$10,000 per year for service as chairman of the Nominating and Corporate Governance Committee;

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- \$10,000 per year for service as non-chairman member of the Audit Committee;
- \$7,500 per year for service as non-chairman member of the Compensation Committee; and
- \$5,000 per year for service as non-chairman member of the Nominating and Corporate Governance Committee.

Non-employee members of our board of directors will also receive automatic grants of non-statutory stock options under our 2014 Plan. For purposes of our automatic director grant program, a non-employee director is a director who is not employed by us and who does not receive compensation from us or have a business relationship with us that would require disclosure under certain SEC rules. Each non-employee director joining our board of directors will automatically be granted a non-statutory stock option to purchase 25,000 shares of common stock with an exercise price equal to the fair market value of our common stock on the grant date. This initial option will vest ratably in annual installments over three years of service following the date of grant.

In addition, on the date of each annual meeting of our stockholders, each non-employee director will automatically be granted a non-statutory stock option to purchase 12,500 shares of our common stock on that date with an exercise price equal to the fair market value of our common stock on the grant date. A non-employee director who receives an initial award will not receive the additional annual award in the same calendar year. Automatic annual grants vest in full on the one-year anniversary of the grant date.

If we are subject to a change in control, then all of the directors' automatic grants will become fully vested. All automatic director options have a maximum term of ten years.

We will also reimburse our non-employee directors for their reasonable out-of-pocket expenses incurred in attending board of directors and committee meetings.

Equity Compensation Plans and Other Benefit Plans***2014 Equity Incentive Award Plan***

We have adopted the 2014 Equity Incentive Award Plan (2014 Plan), which will become effective immediately prior to the effectiveness of the registration statement to which this prospectus relates. The principal purpose of the 2014 Plan is to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards and cash-based performance bonus awards. The material terms of the 2014 Plan, as it is currently contemplated, are summarized below. Our board of directors is still in the process of developing, approving and implementing the 2014 Plan and, accordingly, this summary is subject to change.

Share Reserve

Under the 2014 Plan, 2,088,332 shares of our common stock will be initially reserved for issuance pursuant to a variety of stock-based compensation awards, including stock options, stock appreciation rights (SARs), restricted stock awards, restricted stock unit awards, deferred stock awards, deferred stock unit awards, dividend equivalent awards, stock payment awards and performance awards, plus the number of shares remaining available for future awards under the Amended and Restated 2006 Equity Incentive Plan, as amended (2006 Plan), as of the consummation of this offering. The number of shares initially reserved for issuance or transfer pursuant to awards under the 2014 Plan will be increased by (i) the number of shares represented by awards outstanding under our 2006 Plan, as amended, that are forfeited or lapse unexercised and which following the effective date are not issued under our 2006 Plan and (ii) an annual increase on the first day of each fiscal year beginning in 2014 and ending in 2023, equal to the least of (A) four percent (4%) of the shares of stock outstanding (on an as converted basis) on the last day of the immediately preceding fiscal year and (B) such smaller number of shares of stock as determined by our board of directors; provided, however, that no more than 2,088,332 shares of stock may be issued upon the exercise of incentive stock options (ISOs).

The following counting provisions will be in effect for the share reserve under the 2014 Plan:

- generally, to the extent that an award terminates, expires or lapses for any reason or an award is settled in cash without the delivery of shares, any shares subject to the award at such time will be available for future grants under the 2014 Plan;
- shares tendered to or withheld to satisfy the grant, exercise price or tax withholding obligation with respect to an award under the 2014 Plan and shares subject to a SAR that are not issued in connection with the

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stock settlement of the stock appreciation on exercise thereof may again become available for future grants under the 2014 Plan;

- shares repurchased on the open market with the cash proceeds from the exercise of options will not be available for future grants of awards;
- to the extent that shares of our common stock are repurchased by us prior to vesting so that shares are returned to us, such shares will be available for future grants under the 2014 Plan;
- the payment of dividend equivalents in cash in conjunction with any outstanding awards will not be counted against the shares available for issuance under the 2014 Plan; and
- to the extent permitted by applicable law or any exchange rule, shares issued in assumption of, or in substitution for, any outstanding awards of any entity acquired in any form of combination by us or any of our subsidiaries will not be counted against the shares available for issuance under the 2014 Plan.

In addition, the maximum aggregate value of awards that may be granted to any non-employee director pursuant to the 2014 Plan during any calendar year is \$750,000.

Administration

The compensation committee of our board of directors is expected to administer the 2014 Plan unless our board of directors assumes authority for administration. Unless otherwise determined by our board of directors, the compensation committee will consist of at least two members of our board of directors, each of whom is intended to qualify as an "outside director," within the meaning of Section 162(m) of the Code, a "non-employee director" for purposes of Rule 16b-3 under the Exchange Act and an "independent director" within the meaning of the rules of the applicable stock exchange or other principal securities market on which shares of our common stock are traded. The 2014 Plan provides that the board or compensation committee may delegate its authority to grant awards to employees other than executive officers and certain senior executives of the company to a committee consisting of one or more members of our board of directors or one or more of our officers, other than awards made to our non-employee directors, which must be approved by our full board of directors.

Subject to the terms and conditions of the 2014 Plan, the administrator has the authority to select the persons to whom awards are to be made, to determine the number of shares to be subject to awards and the terms and conditions of awards, and to make all other determinations and to take all other actions necessary or advisable for the administration of the 2014 Plan. The administrator is also authorized to adopt, amend or rescind rules relating to administration of the 2014 Plan. Our board of directors may at any time remove the compensation committee as the administrator and re-vest in itself the authority to administer the 2014 Plan. The full board of directors will administer the 2014 Plan with respect to awards to non-employee directors.

Eligibility

Options, SARs, restricted stock and all other stock-based and cash-based awards under the 2014 Plan may be granted to individuals who are then our officers, employees or consultants or are the officers, employees or consultants of certain of our affiliates. Such awards also may be granted to our directors. Only employees of our company or certain of our affiliates may be granted ISOs.

Awards

The 2014 Plan provides that the administrator may grant or issue stock options, SARs, restricted stock, restricted stock units, deferred stock, deferred stock units, dividend equivalents, performance awards and stock payments, or any combination thereof. Each award will be set forth in a separate agreement with the person receiving the award and will indicate the type, terms and conditions of the award.

- *Nonstatutory stock options (NSOs)* will provide for the right to purchase shares of our common stock at a specified price which may not be less than fair market value on the date of grant, and usually will become exercisable (at the discretion of the administrator) in one or more installments after the grant date, subject to the participant's continued employment or service with us and/or subject to the satisfaction of corporate performance targets and individual performance targets established by the administrator. NSOs may be granted for any term specified by the administrator that does not exceed ten years.
- *Incentive stock options* will be designed in a manner intended to comply with the provisions of Section 422 of the Code and will be subject to specified restrictions contained in the Code. Among such restrictions, ISOs

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must have an exercise price of not less than the fair market value of a share of common stock on the date of grant, may only be granted to employees, and must not be exercisable after a period of ten years measured from the date of grant. In the case of an ISO granted to an individual who owns (or is deemed to own) at least 10% of the total combined voting power of all classes of our capital stock, the 2014 Plan provides that the exercise price must be at least 110% of the fair market value of a share of common stock on the date of grant and the ISO must not be exercisable after a period of five years measured from the date of grant.

- *Restricted stock* may be granted to any eligible individual and made subject to such restrictions as may be determined by the administrator. Restricted stock, typically, may be forfeited for no consideration or repurchased by us at the original purchase price if the conditions or restrictions on vesting are not met. In general, restricted stock may not be sold or otherwise transferred until restrictions are removed or expire. Purchasers of restricted stock, unlike recipients of options, will have voting rights and will have the right to receive dividends, if any, prior to the time when the restrictions lapse, however, extraordinary dividends will generally be placed in escrow, and will not be released until restrictions are removed or expire.
- *Restricted stock units* may be awarded to any eligible individual, typically without payment of consideration, but subject to vesting conditions based on continued employment or service or on performance criteria established by the administrator. Like restricted stock, restricted stock units may not be sold, or otherwise transferred or hypothecated, until vesting conditions are removed or expire. Unlike restricted stock, stock underlying restricted stock units will not be issued until the restricted stock units have vested, and recipients of restricted stock units generally will have no voting or dividend rights prior to the time when vesting conditions are satisfied.
- *Deferred stock awards* represent the right to receive shares of our common stock on a future date. Deferred stock may not be sold or otherwise hypothecated or transferred until issued. Deferred stock will not be issued until the deferred stock award has vested, and recipients of deferred stock generally will have no voting or dividend rights prior to the time when the vesting conditions are satisfied and the shares are issued. Deferred stock awards generally will be forfeited, and the underlying shares of deferred stock will not be issued, if the applicable vesting conditions and other restrictions are not met.
- *Deferred stock units* are denominated in unit equivalent of shares of our common stock, and vest pursuant to a vesting schedule or performance criteria set by the administrator. The common stock underlying deferred stock units will not be issued until the deferred stock units have vested, and recipients of deferred stock units generally will have no voting rights prior to the time when vesting conditions are satisfied.
- *Stock appreciation rights* may be granted in connection with stock options or other awards, or separately. SARs granted in connection with stock options or other awards typically will provide for payments to the holder based upon increases in the price of our common stock over a set exercise price. The exercise price of any SAR granted under the 2014 Plan must be at least 100% of the fair market value of a share of our common stock on the date of grant. Except as required by Section 162(m) of the Code with respect to a SAR intended to qualify as performance based compensation as described in Section 162(m) of the Code, there are no restrictions specified in the 2014 Plan on the exercise of SARs or the amount of gain realizable therefrom, although restrictions may be imposed by the administrator in the SAR agreements. SARs under the 2014 Plan will be settled in cash or shares of our common stock, or in a combination of both, at the election of the administrator.
- *Dividend equivalents* represent the value of the dividends, if any, per share paid by us, calculated with reference to the number of shares covered by the award. Dividend equivalents may be settled in cash or shares and at such times as determined by the compensation committee or board of directors, as applicable.
- *Performance awards* may be granted by the administrator on an individual or group basis. Generally, these awards will be based upon specific performance targets and may be paid in cash or in common stock or in a combination of both. Performance awards may include "phantom" stock awards that provide for payments based upon the value of our common stock. Performance awards may also include bonuses that may be granted by the administrator on an individual or group basis and which may be payable in cash or in common stock or in a combination of both.
- *Stock payments* may be authorized by the administrator in the form of common stock or an option or other right to purchase common stock as part of a deferred compensation or other arrangement in lieu of all or any part of compensation, including bonuses, that would otherwise be payable in cash to the employee, consultant or non-employee director.

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In the event of a change in control where the acquiror does not assume or replace awards granted, prior to the consummation of such transaction, awards issued under the 2014 Plan, other than performance awards, will be subject to accelerated vesting such that 100% of such awards will become vested and exercisable or payable, as applicable. Performance awards will vest in accordance with the terms and conditions of the applicable award agreement. In addition, the administrator will also have complete discretion to structure one or more awards under the 2014 Plan to provide that such awards will become vested and exercisable or payable on an accelerated basis in the event such awards are assumed or replaced with equivalent awards but the individual's service with us or the acquiring entity is subsequently terminated within a designated period following the change in control event. The administrator may also make appropriate adjustments to awards under the 2014 Plan and is authorized to provide for the acceleration, cash-out, termination, assumption, substitution or conversion of such awards in the event of a change in control or certain other unusual or nonrecurring events or transactions. Under the 2014 Plan, a change in control is generally defined as:

- the transfer or exchange in a single transaction or series of related transactions by our stockholders of more than 50% of our voting stock to a person or group;
- a change in the composition of our board of directors over a two-year period such that the members of the board of directors who were approved by at least two-thirds of the directors who were directors at the beginning of the two year period or whose election or nomination was so approved cease to constitute a majority of the board of directors;
- the consummation of a merger, consolidation, reorganization or business combination, sale or disposition of all or substantially all of our assets, or acquisition of assets or stock of another entity, in each case, other than a transaction that results in our outstanding voting securities immediately before the transaction continuing to represent a majority of the voting power of the acquiring company's outstanding voting securities and after which no person or group beneficially owns 50% or more of the outstanding voting securities of the surviving entity immediately after the transaction; or
- stockholder approval of our liquidation or dissolution.

Adjustments of Awards

In the event of a nonreciprocal transaction between the company and its stockholders, such as a stock dividend, stock split, spin-off, rights offering or recapitalization affecting the number of outstanding shares of our common stock or the share price of our common stock, the administrator will make appropriate, proportionate adjustments to:

- the aggregate number and type of shares subject to the 2014 Plan;
- the number and kind of shares subject to outstanding awards and terms and conditions of outstanding awards (including, without limitation, any applicable performance targets or criteria with respect to such awards); and
- the grant or exercise price per share of any outstanding awards under the 2014 Plan.

In the event of certain other corporate transactions, in order to prevent dilution or enlargement of the potential benefits intended to be made available under the 2014 Plan, the administrator has the discretion to make such equitable adjustments and may also:

- provide for the termination or replacement of an award in exchange for cash or other property;
- provide that any outstanding award cannot vest, be exercised or become payable after such event;
- provide that awards may be exercisable, payable or fully vested as to shares of common stock covered thereby; or
- provide that any surviving corporation will assume or substitute outstanding awards under the 2014 Plan.

Amendment and Termination

Our board of directors or the compensation committee may terminate, amend or modify the 2014 Plan at any time and from time to time. However, we must generally obtain stockholder approval:

- to increase the number of shares available under the 2014 Plan (other than in connection with certain corporate events, as described above);

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- reduce the price per share of any outstanding option or SAR granted under the 2014 Plan; or
- cancel any option or SAR in exchange for cash or another award when the option or stock appreciation right price per share exceeds the fair market value of the underlying shares.

Termination

The board of directors may terminate the 2014 Plan at any time. No awards may be granted pursuant to the 2014 Plan after the tenth anniversary of the effective date of the 2014 Plan. Any award that is outstanding on the termination date of the 2014 Plan will remain in force according to the terms of the 2014 Plan and the applicable award agreement.

We intend to file with the SEC a registration statement on Form S-8 covering the shares of our common stock issuable under the 2014 Plan.

2014 Employee Stock Purchase Plan

We have adopted an employee stock purchase plan (ESPP), which will be effective immediately prior to the effectiveness of the registration statement to which this prospectus relates. The first offering period under the ESPP will commence on a date to be determined by our compensation committee, in its discretion. The ESPP is designed to allow our eligible employees and the eligible employees of our participating subsidiaries to purchase shares of our common stock, at semi-annual intervals, with their accumulated payroll deductions. The ESPP is intended to qualify under Section 423 of the Code.

Plan Administration. Subject to the terms and conditions of the ESPP, our compensation committee will administer the ESPP; our compensation committee can delegate administrative tasks under the ESPP to the services of an agent and/or employees to assist in the administration of the ESPP. The administrator will have the discretionary authority to administer and interpret the ESPP. The administrator's interpretations and constructions of any provision of the ESPP or any rights thereunder will be conclusive and binding on all persons. We will bear all expenses and liabilities incurred by the ESPP administrator.

Shares Available Under the ESPP. The maximum number of our shares of our common stock which will be authorized for sale under the ESPP is equal to the sum of (a) 208,833 shares of common stock and (b), if approved by our compensation committee, an annual increase on the first day of each year beginning in 2015 and ending in 2024, equal to the lesser of (i) one percent (1%) of the shares of common stock outstanding (on an as converted basis) on the last day of the immediately preceding fiscal year and (ii) such number of shares of common stock as determined by our board of directors; provided, however, that no more than 3.0 million shares of common stock can be issued under the ESPP. The shares made available for sale under the ESPP may be authorized but unissued shares or reacquired shares reserved for issuance under the ESPP.

Eligible Employees. Employees eligible to participate in the ESPP generally include employees who are employed by us or one of our subsidiaries on the first trading day of an offering period, or the enrollment date.

Our employees and any employees of our subsidiaries who customarily work less than five months in a calendar year or are customarily scheduled to work less than 20 hours per week will not be eligible to participate in the ESPP. Finally, an employee who owns (or is deemed to own through attribution) 5% or more of the combined voting power or value of all classes of stock of our company or one of our subsidiaries will not be allowed to participate in the ESPP.

Participation. Employees will enroll under the ESPP by completing a payroll deduction form permitting the deduction of at least 1% from their compensation (but not more than the lesser of 15% of their compensation or \$25,000), and the accumulated deductions will be applied to the purchase of shares on each semi-annual purchase date. Payroll deductions may be expressed as either a whole number percentage or a fixed dollar amount. However, a participant may not purchase more than 5,000 shares in each offering period. The ESPP administrator has the authority to change these limitations for any subsequent offering period.

Offering. Under the ESPP, participants are offered the option to purchase shares of our common stock at a discount during a series of successive offering periods. The first offering period under the ESPP will commence on a date to be determined by our compensation committee, in its discretion. Unless otherwise determined by the ESPP administrator or our board of directors, each offering period will have a duration of six months. However, in no event may an offering period be longer than 27 months in length.

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The option purchase price will be the lower of 85% of the closing trading price per share of our common stock on the first trading day of an offering period in which a participant is enrolled or 85% of the closing trading price per share of our common stock on the semi-annual purchase date, which will occur on the last trading day of each offering period.

Unless a participant has previously canceled his or her participation in the ESPP before the purchase date, the participant will be deemed to have exercised his or her option in full as of each purchase date. Upon exercise, the participant will purchase the number of whole shares that his or her accumulated payroll deductions will buy at the option purchase price, subject to the participation limitations described above.

A participant may cancel his or her payroll deduction authorization at any time prior to the end of the offering period. Upon cancellation, the participant will have the option to either (a) receive the participant's account balance, which will be refunded in cash without interest or (b) exercise the participant's option for the current offering period for the maximum number of shares of common stock on the applicable purchase date, with the remaining account balance refunded in cash without interest. Following at least one payroll deduction, a participant may also decrease (but not increase) his or her payroll deduction authorization once during any offering period. If a participant wants to increase or decrease the rate of payroll withholding, he or she may do so by submitting a new form before the offering period for which such change is to be effective.

A participant may not assign, transfer, pledge or otherwise dispose of (other than by will or the laws of descent and distribution) any rights to exercise an option or to receive shares of our common stock under the ESPP, and during a participant's lifetime, options in the ESPP shall be exercisable only by such participant. Any such attempt at assignment, transfer, pledge or other disposition will not be given effect.

Adjustments upon Changes in Recapitalization, Dissolution, Liquidation, Merger or Asset Sale. In the event of any increase or decrease in the number of issued shares of our common stock resulting from a stock split, reverse stock split, stock dividend, combination or reclassification of the common stock, or any other increase or decrease in the number of shares of common stock effected without receipt of consideration by us, we will proportionately adjust the aggregate number of shares of our common stock offered under the ESPP, the number and price of shares which any participant has elected to purchase pursuant to the ESPP and the maximum number of shares which a participant may elect to purchase in any single offering period.

If there is a proposal to dissolve or liquidate our company, then the ESPP will terminate immediately prior to the consummation of such proposed dissolution or liquidation, and any offering period then in progress will be shortened by setting a new exercise date to take place before the date of our dissolution or liquidation. We will notify each participant of such change in writing at least ten business days prior to the new exercise date. If we undergo a merger with or into another corporation or sale of all or substantially all of our assets, each outstanding option will be assumed or an equivalent option substituted by the successor corporation or the parent or subsidiary of the successor corporation. If the successor corporation refuses to assume the outstanding options or substitute equivalent options, then any offering period then in progress will be shortened by setting a new exercise date to take place before the date of our proposed sale or merger. We will notify each participant of such change in writing at least ten business days prior to the new exercise date.

Amendment and Termination. Our board of directors may amend, suspend or terminate the ESPP at any time. However, we must obtain stockholder approval to increase the number of shares available under the ESPP (other than in connection with certain corporate events). Unless it is sooner terminated by our board of directors, the ESPP will terminate upon the date on which all shares available for issuance under the ESPP shall have been sold pursuant to options exercised under the ESPP. However, our board of directors may not amend the ESPP without obtaining stockholder approval within 12 months before or after such amendment to the extent required by applicable laws.

We intend to file with the SEC a registration statement on Form S-8 covering the shares of our common stock issuable under the ESPP.

Amended and Restated 2006 Equity Incentive Plan

Our board of directors adopted, and our stockholders approved, the 2006 Plan on December 29, 2006. The 2006 Plan was subsequently amended on November 15, 2012 and April 14, 2014. The 2006 Plan provides for the grant

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of ISOs, NSOs, restricted stock units, restricted stock awards, and SARs. As of March 31, 2014, options to purchase 4,134,200 shares of our common stock at a weighted-average exercise price per share of \$0.47 remained outstanding under the 2006 Plan. As of March 31, 2014, 105,800 shares of our common stock were available for future issuance pursuant to awards granted under the 2006 Plan. Following the completion of this offering and in connection with the effectiveness of our 2014 Plan, the 2006 Plan will terminate and no further awards will be granted under the 2006 Plan. However, all outstanding awards will continue to be governed by their existing terms.

Administration

Our board of directors, or a committee thereof appointed by our board of directors, has the authority to administer the 2006 Plan and the awards granted under it. In addition, the administrator may delegate to one or more officers the authority to grant options and other stock awards to participants who are not officers, subject to applicable laws. The administrator has the authority to select the participants to whom awards will be granted under the 2006 Plan, the number of shares to be subject to those awards under the 2006 Plan, and the terms and conditions of the awards granted. In addition, the administrator has the authority to construe and interpret the 2006 Plan and to establish, amend and revoke rules for its administration.

Awards

The 2006 Plan provides that the administrator may grant or issue options, including ISOs and non-qualified stock options, restricted stock awards, restricted stock units and SARs. Each award will be set forth in a separate agreement with the person receiving the award and will indicate the type, terms and conditions of the award.

- *Stock options.* The 2006 Plan provides for the grant of ISOs or NSOs. ISOs may be granted only to employees. NSOs may be granted to employees, directors or consultants. The exercise price of ISOs granted to employees who at the time of grant own stock representing more than 10% of the voting power of all classes of our common stock may not be less than 110% of the fair market value per share of our common stock on the date of grant, and the exercise price of ISOs granted to any other employees may not be less than 100% of the fair market value per share of our common stock on the date of grant. The exercise price of NSOs to employees, directors or consultants may not be less than 100% of the fair market value per share of our common stock on the date of grant. Shares subject to options under the 2006 Plan generally vest in a series of installments over an optionee's period of service.

In general, the maximum term of options granted is ten years. The maximum term of ISOs granted to an employee who owns stock representing more than 10% of the voting power of all classes of our common stock is five years.

- *Restricted stock awards.* The 2006 Plan provides that we may issue restricted stock awards. Each restricted stock award will be governed by a restricted stock award agreement. Generally, upon the participant's termination of service, any unvested restricted stock award will be forfeited. In general, restricted stock may not be sold or otherwise transferred until restrictions are removed or expire. Purchasers of restricted stock, unlike recipients of options, will have voting rights and will have the right to receive dividends, if any, prior to the time when the restrictions lapse.

Adjustments

In the event certain changes with respect to our common stock without the receipt of consideration by the Company, such as through a merger, consolidation, capitalization, stock dividend or stock split, our board of directors will appropriately adjust: (i) the class and maximum number of securities subject to the 2006 Plan; (ii) the class and maximum number of securities that may be issued pursuant to the exercise of ISOs; and (iii) the class, number of securities and price per share of stock subject to outstanding awards. If the company undergoes a dissolution or liquidation, all outstanding awards will terminate immediately prior to the completion of such transaction, and the shares of common stock subject to the company's repurchase option may be repurchased by the company. In the event of certain corporate transactions, including certain sales of the company's assets and certain mergers, if the surviving corporation does not assume, continue or substitute awards under the 2006 Plan, then such awards shall vest in full to a date prior to the effective time of the transaction and the awards will terminate if not exercised prior to the effective time of the transaction. Awards under the 2006 Plan may be subject to additional acceleration of vesting and exercisability upon or after a change in control as provided in the applicable award agreement, but in the absence of such provision, no acceleration shall occur.

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The board of directors may amend, modify or terminate the 2006 Plan at any time. However, except in connection with certain changes in the company's capital structure and to the extent required by applicable law, stockholder approval will be required for an amendment that (i) materially increases the number of shares of common stock issuable under the 2006 Plan; (ii) materially expands the class of individuals eligible to receive awards under the 2006 Plan; (iii) materially increases the benefits accruing to participants under the 2006 Plan or materially reduces the price at which shares of common stock may be issued or purchased under the 2006 Plan; (iv) materially extends the term of the 2006 Plan or (v) expands the types of awards issuable under the 2006 Plan. Generally, no amendment may impair the rights of a holder of an outstanding award without the holder's consent. Following the completion of this offering and in connection with the effectiveness of our 2014 Plan, the 2006 Plan will terminate and no further awards will be granted under the 2006 Plan.

We intend to file with the SEC a registration statement on Form S-8 covering the shares of our common stock issuable under the 2006 Plan.

401(k) Plan

Our U.S. eligible employees, including our NEOs, participate in a defined-contribution savings plan under Section 401(k) of the Code (401(k) Plan). Enrollment in the 401(k) Plan is automatic for employees who meet eligibility requirements unless they decline participation. Under the 401(k) Plan, we provide non-elective safe harbor contributions of 3% of a plan participant's annual compensation. The maximum employee contribution to the 401(k) Plan is \$17,500 for 2013 and 2014 tax years based on IRS guidelines for all employees with an additional \$5,500 for additional catch-up contributions for plan participants age 50 and older, subject to regulatory and plan limitations.

Rule 10b5-1 Sales Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. The director or officer may amend or terminate the plan in limited circumstances. Our directors and executive officers may also buy or sell additional shares of our common stock outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

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The following is a description of transactions since January 1, 2011 to which we have been a party, in which the amount involved exceeds \$120,000, and in which any of our directors, executive officers or holders of more than 5% of our capital stock, or an affiliate or immediate family member thereof, had or will have a direct or indirect material interest.

Participation in this Offering

Certain of our existing investors have indicated an interest in purchasing an aggregate of approximately \$30.0 million of shares of the common stock in this offering on the same terms as those offered to the public. However, indications of interest are not binding agreements or commitments to purchase and any of these entities may determine to purchase more, fewer or no shares in this offering.

Repurchase of Series A Convertible Preferred Stock

In April 2014, we repurchased an aggregate of 531,208 shares of our Series A convertible preferred stock from Zygtech, LLC at a price per share of \$7.53 for an aggregate purchase price of approximately \$4.0 million.

Issuance of Series B Convertible Preferred Stock

In April 2014, we issued an aggregate of 7,321,003 shares of our Series B convertible preferred stock for an aggregate purchase price of approximately \$55 million, which included conversion of the aggregate \$2.0 million principal amount on outstanding convertible promissory notes described below. The table below sets forth the number of shares of Series B convertible preferred stock sold to our directors, executive officers, then 5% stockholders and their affiliates. Upon completion of this offering, each share of Series B convertible preferred stock will convert into one share of Common Stock.

NAME	NUMBER OF SHARES OF SERIES B PREFERRED STOCK	AGGREGATE PURCHASE PRICE
Regeneron Pharmaceuticals, Inc.	531,208	\$ 3,999,996
Zygtech, LLC.	295,115	\$ 2,222,216
Wachter Family Trust ⁽¹⁾	63,081	\$ 475,000
John P. McLaughlin ⁽²⁾	26,560	\$ 199,997
Hans P. Hull ⁽³⁾	3,320	\$ 25,000

⁽¹⁾ Paul D. Wachter, a member of our board of directors, is a trustee of the Wachter Family Trust.

⁽²⁾ John P. McLaughlin is a member of our board of directors.

⁽³⁾ Hans P. Hull is one of our named executive officers.

Issuance of Series A Convertible Preferred Stock

In November 2013, we issued an aggregate of 2,109,614 shares of our Series A convertible preferred stock at a price per share of \$1.45 for an aggregate purchase price of approximately \$3.1 million, which included conversion of the aggregate principal amount and accrued interest on convertible promissory notes described below. The table below sets forth the number of shares of Series A convertible preferred stock sold to our then 5% stockholders and their affiliates. Upon completion of this offering, each share of Series A convertible preferred stock will convert into one share of Common Stock.

NAME	NUMBER OF SHARES OF SERIES A PREFERRED STOCK	AGGREGATE PURCHASE PRICE
Zygtech, LLC.	1,419,959	\$ 2,058,944
Regeneron Pharmaceuticals, Inc.	689,655	\$ 1,000,000

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In October 2013, we entered into a Note Purchase Agreement with Zytech, LLC pursuant to which we issued unsecured subordinated convertible promissory notes in an aggregate principal amount of \$2.0 million. Such convertible promissory notes were subordinate to certain senior indebtedness and accrued interest at the rate of 5% per annum, compounded annually. In April 2014, the aggregate principal amount of the convertible promissory notes converted into 295,115 shares of our Series B convertible preferred stock at a price of \$6.78 per share.

In August 2012, we entered into a Note Purchase Agreement with Zytech, LLC pursuant to which we issued unsecured subordinated convertible promissory notes in an aggregate principal amount of \$2.0 million. Such convertible promissory notes were subordinate to certain senior indebtedness and accrued interest at the rate of 5% per annum, compounded annually. In November 2013, the aggregate principal amount and accrued interest on such convertible promissory notes converted into 1,419,959 shares of our Series A convertible preferred stock as described above.

Relationship with Regeneron and Concurrent Private Placement

In May 2014, we entered into a research collaboration and license agreement with Regeneron. See "Business—Regeneron." Pursuant to the collaboration, we received initial payments of \$8.0 million in May 2014.

Regeneron has agreed to purchase approximately \$10.0 million of our common stock in a separate private placement concurrent with the completion of this offering at a price per share equal to the public offering price. The sale of such shares will not be registered under the Securities Act. The closing of this offering is not conditioned upon the closing of such concurrent private placement.

Investor Rights Agreement

We and the holders of our Series A and Series B convertible preferred stock have entered into an amended and restated investor rights agreement, as amended, pursuant to which these stockholders and warrant holders will have, among other things, registration rights under the Securities Act with respect to their shares of common stock following this offering. Prior to the completion of this offering, all outstanding shares of our convertible preferred stock will be converted into common stock. See "Description of Capital Stock—Registration Rights" for more information about the investors rights agreement.

Voting Agreement

Pursuant to an amended and restated voting agreement that we entered into with certain holders of our common stock and certain holders of our convertible preferred stock:

- the holders of a majority of our Series A convertible preferred stock, voting separately as a single class, have the right to elect one director to our board of directors, for which Dr. Schwartz has been designated;
- our then-incumbent Chief Executive Officer has the right to be nominated to serve on our board of directors; and
- the holders of a majority of our common stock, voting separately as a single class, have the right to elect one director to our board of directors, for which Dr. Blumenkranz has been designated.

The holders of our common stock and convertible preferred stock who are parties to the amended and restated voting agreement, as amended, are obligated to vote for such designees. The provisions of this voting agreement will terminate upon the consummation of this offering and there will be no further contractual obligations regarding the election of our directors. Our directors hold office until their successors have been elected and qualified or appointed, or the earlier of their death, resignation or removal.

Right of First Refusal and Co-Sale Agreement

We have entered into a right of first refusal and co-sale agreement with certain holders of our common stock and holders of our convertible preferred stock. This agreement provides for rights of first refusal and co-sale relating to the shares of our common stock held by certain key holders of our common stock. Upon the closing of this offering, the amended and restated right of first refusal and co-sale agreement will terminate.

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Director and Executive Officer Compensation

Please see “Executive and Director Compensation” for information regarding compensation of directors and executive officers.

Employment Agreements

We have entered into employment agreements with our executive officers. For more information regarding these agreements, see “Executive and Director Compensation—Narrative to Summary Compensation Table and Outstanding Equity Awards at 2013 Fiscal Year End.”

Indemnification Agreements and Directors’ and Officers’ Liability Insurance

We intend to enter into indemnification agreements with each of our directors and executive officers prior to the consummation of this offering. These agreements, among other things, require us or will require us to indemnify each director (and in certain cases their related venture capital funds) and executive officer to the fullest extent permitted by Delaware law, including indemnification of expenses such as attorneys’ fees, judgments, fines and settlement amounts incurred by the director or executive officer in any action or proceeding, including any action or proceeding by or in right of us, arising out of the person’s services as a director or executive officer.

Policies and Procedures for Related Party Transactions

Our board of directors has adopted a written related person transaction policy to set forth the policies and procedures for the review and approval or ratification of related person transactions. This policy will cover, with certain exceptions set forth in Item 404 of Regulation S-K, any transaction, arrangement or relationship, or any series of similar transactions, arrangements or relationships in which we were or are to be a participant, where the amount involved exceeds \$120,000 and a related person had, has or will have a direct or indirect material interest, including, without limitation, purchases of goods or services by or from the related person or entities in which the related person has a material interest, indebtedness, guarantees of indebtedness and employment by us of a related person.

As provided by our audit committee charter to be effective upon consummation of this offering, our audit committee will be responsible for reviewing and approving in advance the related party transactions covered by the company’s related transaction policies and procedures.

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Table of Contents**PRINCIPAL STOCKHOLDERS**

The following table sets forth information relating to the beneficial ownership of our common stock as of June 30, 2014, by:

- each person, or group of affiliated persons, known by us to beneficially own more than 5% of our outstanding shares of common stock;
- each of our directors;
- each of our named executive officers; and
- all directors and current executive officers as a group.

The number of shares beneficially owned by each entity, person, director or executive officer is determined in accordance with the rules of the SEC, and the information is not necessarily indicative of beneficial ownership for any other purpose. Under such rules, beneficial ownership includes any shares over which the individual has sole or shared voting power or investment power as well as any shares that the individual has the right to acquire within 60 days of June 30, 2014 through the exercise of any stock option, warrants or other rights. Except as otherwise indicated, and subject to applicable community property laws, the persons named in the table have sole voting and investment power with respect to all shares of common stock held by that person.

The percentage of shares beneficially owned is computed on the basis of 14,769,043 shares of our common stock outstanding as of June 30, 2014, which assumes (i) the conversion of all outstanding shares of convertible preferred stock as of June 30, 2014 into 10,689,027 shares of common stock, and (ii) the issuance of 407,131 shares of common stock upon the cash exercise of outstanding in-the-money warrants which would otherwise expire in connection with this offering. For purposes of the column "Percentage of Shares Beneficially Owned—After Offering," we have assumed that 20,775,103 shares of common stock will be issued and outstanding upon completion of this offering and the concurrent private placement of \$10.0 million of common stock to Regeneron (or 606,060 shares assuming such shares are sold to Regeneron at \$16.50 per share, the mid-point of the price range on the cover this prospectus). Except with respect to the warrants described above (which shares are assumed to be issued and outstanding), shares of our common stock that a person has the right to acquire within 60 days of June 30, 2014 are deemed outstanding for purposes of computing the percentage ownership of the person holding such rights, but are not deemed outstanding for purposes of computing the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers as a group. Unless otherwise indicated below, the address for each beneficial owner listed is c/o Avalanche Biotechnologies, Inc., at 1035 O'Brien Drive, Suite A, Menlo Park, CA 94025.

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Certain of our existing investors have indicated an interest in purchasing an aggregate of approximately \$30.0 million of shares of the common stock in this offering on the same terms as those offered to the public. However, indications of interest are not binding agreements or commitments to purchase and any of these entities may determine to purchase more, fewer or no shares in this offering. Any amounts that may be purchased by these investors in this offering have not been included in the following table.

NAME OF BENEFICIAL OWNER	NUMBER OF SHARES BENEFICIALLY OWNED		PERCENTAGE OF SHARES BENEFICIALLY OWNED	
	BEFORE OFFERING	AFTER OFFERING	BEFORE OFFERING	AFTER OFFERING
5% and Greater Stockholders				
Zytech, LLC ⁽¹⁾	2,563,176	2,563,176	17.4%	12.3%
Entities affiliated with Venrock ⁽²⁾	1,965,471	1,965,471	13.4%	9.5%
Entities affiliated with FMR, LLC ⁽³⁾	1,328,021	1,328,021	9.0%	6.4%
Regeneron Pharmaceuticals, Inc.	1,220,863	1,826,923	8.2%	8.8%
Entities affiliated with Deerfield Management Company, L.P. ⁽⁴⁾	863,212	863,212	5.9%	4.2%
Named Executive Officers and Directors				
Thomas W. Chalberg, Jr., Ph.D. ⁽⁵⁾	1,765,988	1,765,988	11.6%	8.3%
Linda C. Bain	—	—	—	—
Hans Hull.	65,195	65,195	*	*
Mehdi Gasmî, Ph.D.	—	—	—	—
Mark S. Blumenkranz, M.D. ⁽⁶⁾	1,053,582	1,053,582	7.0%	5.0%
John P. McLaughlin	35,935	35,935	*	*
Steven D. Schwartz, M.D.	894,931	894,931	6.0%	4.2%
Paul D. Wachter	72,456	72,456	*	*
All directors and current executive officers as a group (9 persons)	3,888,087	3,888,087	24.4%	17.7%

* Indicates beneficial ownership of less than 1% of the total outstanding common stock.

(1) Voting and dispositive rights held by Zygmunt Wilf, Mark Wilf and Jonathan Wilf.

(2) Includes (i) 911,193 shares held by Venrock Associates VI, L.P. (VA VI), (ii) 830,805 shares held by Venrock Healthcare Capital Partners, L.P. (VHCP), (iii) 71,543 shares held by Venrock Partners VI, L.P. (VP VI) and (iv) 151,930 shares held by VHCP Co-Investment Holdings, LLC. (VHCP Co.). Venrock Management VI, LLC (VM VI), a Delaware limited liability company, is the sole General Partner of VA VI. Venrock Partners Management VI, LLC (VPM VI), a Delaware limited liability company, is the sole general partner of VP VI. VHCP Management, LLC (VHCPM), a Delaware limited liability company, is the sole general partner of VHCP and manager of VHCP Co. VM VI, VPM VI, and VHCPM expressly disclaim beneficial ownership over all shares held by VA VI, VP VI, VHCP and VHCP Co., except to the extent of their indirect pecuniary interest therein. Bryan E. Roberts and Anders D. Hove are the sole voting members of VHCPM and disclaim beneficial ownership over all shares held by VHCP and VHCP Co., except to the extent of their indirect pecuniary interest therein. The address of Venrock is 3340 Hillview Avenue, Palo Alto, California 94304.

(3) Includes (i) 89,832 shares held by Bangle & Co fbo Fidelity Advisor Series VII: Fidelity Advisor Biotechnology Fund, (ii) 700,821 shares held by Booth & Co fbo Fidelity Securities Fund: Fidelity OTC Portfolio and (iii) 537,368 shares held by Mag & Co fbo Fidelity Select Portfolios: Biotechnology Portfolio. Fidelity Management & Research Company (Fidelity), 82 Devonshire Street, Boston, Massachusetts 02109, a wholly-owned subsidiary of FMR LLC and an investment adviser registered under Section 203 of the Investment Advisers Act of 1940, is the beneficial owner of 1,328,021 Shares of Avalanche Biotechnologies, Inc. (Company) as a result of acting as investment adviser to various investment companies registered under Section 8 of the Investment Company Act of 1940. Edward C. Johnson 3d and FMR LLC, through its control of Fidelity, and the funds each has sole power to dispose of the 1,328,021 Shares owned by the Funds. Members of the family of Edward C. Johnson 3d, Chairman of FMR LLC, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Edward C. Johnson 3d, Chairman of FMR LLC, has the sole power to vote or direct the voting of the shares owned directly by the Fidelity Funds, which power resides with the Funds' Boards of Trustees. Fidelity carries out the voting of the shares under written guidelines established by the Funds' Boards of Trustees.

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- (4) Includes (i) 531,208 shares held by Deerfield Private Design Fund III, L.P., (ii) 184,594 shares held by Deerfield Special Situations Fund, L.P. and (iii) 147,410 shares held by Deerfield Special Situations International Master Fund, L.P. Deerfield Mgmt, L.P. is the general partner of each of Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P. Deerfield Mgmt III, L.P. is the general partner of Deerfield Private Design Fund III, L.P. (together with Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P., the Deerfield Funds). Deerfield Management Company, L.P. is the investment manager of each of the Deerfield Funds. Mr. James E. Flynn is the sole member of the general partner of each of Deerfield Mgmt, L.P., Deerfield Mgmt III, L.P. and Deerfield Management Company, L.P. Deerfield Mgmt, L.P. may be deemed to beneficially own the shares held by Deerfield Special Situations Fund, L.P. and Deerfield Special Situations International Master Fund, L.P. Deerfield Mgmt III, L.P. may be deemed to beneficially own the shares held by Deerfield Private Design Fund III, L.P. Each of Deerfield Management Company, L.P. and Mr. Flynn may be deemed to beneficially own the shares held by the Deerfield Funds. The address of the Deerfield Funds is c/o Deerfield Management Company, L.P., 780 Third Avenue, 37th Floor, New York, NY 10017.
- (5) Includes (i) 367,886 shares held and 483,102 shares that may be acquired pursuant to the exercise of options held prior to this offering by Thomas W. Chalberg, Jr., Ph.D.; (ii) 420,000 shares held by Stefanie R. Chalberg 2014 Grantor Retained Annuity Trust under agreement Dated April 30, 2014; and (iii) 420,000 shares held by Thomas W. Chalberg, Jr., Ph.D. as trustee of the Thomas W. Chalberg 2014 Grantor Retained Annuity Trust under agreement Dated April 30, 2014.
- (6) Includes (i) 8,394 shares held and 4,137 shares that may be acquired pursuant to the exercise of warrants held prior to this offering by Carla Helene Blumenkranz Irrevocable Trust; (ii) 8,394 shares held and 4,137 shares that may be acquired pursuant to the exercise of warrants held prior to this offering by Erik Davis Blumenkranz Irrevocable Trust; and (iii) 8,394 shares held and 4,137 shares that may be acquired pursuant to the exercise of warrants held prior to this offering by Scott Aubrey Blumenkranz Irrevocable Trust.

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[Table of Contents](#)**DESCRIPTION OF CAPITAL STOCK**

The following summary describes our capital stock and the material provisions of our amended and restated certificate of incorporation and our amended and restated bylaws, which will become effective upon the closing of this offering, the amended and restated investor rights agreement to which we and certain of our stockholders are parties and of the Delaware General Corporation Law. Because the following is only a summary, it does not contain all of the information that may be important to you. For a complete description, you should refer to our amended and restated certificate of incorporation, amended and restated bylaws and amended and restated investor rights agreement, copies of which have been filed as exhibits to the registration statement of which this prospectus is part.

General

Upon the consummation of this offering, we will have authorized under our amended and restated certificate of incorporation 300,000,000 shares of common stock, \$0.0001 par value per share, and 5,000,000 shares of preferred stock, \$0.0001 par value per share.

As of March 31, 2014, there were 3,672,885 shares of our common stock outstanding held by 13 stockholders of record, outstanding options to purchase 4,134,200 shares of common stock and outstanding warrants to purchase 289,000 shares of common stock.

Common Stock**Voting Rights**

Each holder of our common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors. In the election of directors, a plurality of the votes cast at a meeting of stockholders is sufficient to elect a director. Our stockholders do not have cumulative voting rights in the election of directors. Accordingly, holders of a majority of the voting shares are able to elect all of the directors. In all other matters, except as noted below under “—Amendment of our Amended and Restated Certificate of Incorporation or our Amended and Restated Bylaws” and “—Election and Removal of Directors” and except where a higher threshold is required by law, a majority of the votes cast affirmatively or negatively (excluding abstentions and broker non-votes) will decide such matters.

Dividends

Subject to preferences that may be applicable to any then outstanding preferred stock, holders of our common stock are entitled to receive dividends, if any, as may be declared from time to time by our board of directors out of legally available funds.

Liquidation

In the event of our liquidation, dissolution or winding up, holders of our common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any then outstanding shares of preferred stock.

Other Rights and Preferences

Holders of our common stock have no preemptive, conversion, subscription or other rights, and there are no redemption or sinking fund provisions applicable to our common stock. The rights, preferences and privileges of the holders of our common stock are subject to and may be adversely affected by the rights of the holders of shares of any series of preferred stock that we may designate in the future.

Preferred Stock

Upon the consummation of this offering, our board of directors will have the authority, without further action by our stockholders, to issue up to 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions thereof. These rights, preferences and privileges could include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of such series, any or all of which may be greater than

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the rights of common stock. The issuance of our preferred stock could adversely affect the voting power of holders of common stock and the likelihood that such holders will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying, deferring or preventing a change of control of our company or other corporate action. Upon consummation of this offering, no shares of preferred stock will be outstanding, and we have no present plan to issue any shares of preferred stock.

Warrants

The following table sets forth information about outstanding warrants to purchase shares of our stock immediately prior to the consummation of this offering.

CLASS OF STOCK	SHARES EXERCISABLE PRIOR TO THIS OFFERING	SHARES OF COMMON STOCK EXERCISABLE FOLLOWING THIS OFFERING	EXERCISE PRICE/SHARE	EXPIRATION DATE
Preferred Stock	54,716	—	\$ 1.45	(1)
Common Stock	352,415	—	\$ 1.49	(1)

(1) If the warrants are not exercised in connection with the offering, they will expire.

Registration Rights

We are party to an amended and restated investor rights agreement, which provides certain of our preferred stockholders the right to demand that we file a registration statement for their shares of common stock or request that their shares of common stock be covered by a registration statement that we are otherwise filing, in each case, to the extent their shares of common stock were issued upon conversion of convertible preferred stock. These shares are referred to as registrable securities.

Demand Registration Rights

The holders of registrable securities are entitled to certain demand registration rights. At any time beginning on the earlier of April 16, 2017 and 180 days following the completion of this offering, the holders of at least 20% of the registrable securities, on not more than two occasions, may request that we register all or a portion of their shares, subject to certain specified exceptions. Such request for registration must cover securities the aggregate offering price of which, before payment of underwriting discounts and commissions, exceeds \$10.0 million.

Piggyback Registration Rights

In connection with this offering, the holders of registrable securities were entitled to, and the necessary percentage of holders waived, their rights to notice of this offering and to include their shares of registrable securities in this offering. If we propose to register for offer and sale any of our securities under the Securities Act in another offering, either for our own account or for the account of other security holders, the holders of these shares will be entitled to certain "piggyback" registration rights allowing them to include their shares in such registration, subject to certain marketing and other limitations. As a result, whenever we propose to file a registration statement under the Securities Act, including a registration statement on Form S-3 as discussed below, other than with respect to (i) any employee benefit plan, (ii) with respect to any corporate reorganization or transaction under Rule 145 of the Securities Act, any registration statements related to the issuance or resale of securities issued in such a transaction or (iii) a registration related to stock issued upon conversion of debt securities, the holders of these shares are entitled to notice of the registration and have the right, subject to limitations that the underwriters may impose on the number of shares included in the registration, to include their shares in the registration.

Form S-3 Registration Rights

The holders of registrable securities are entitled to certain Form S-3 registration rights. Any holder of these shares can make a request that we register for offer and sale their shares on Form S-3 if we are qualified to file a registration statement on Form S-3, subject to certain specified exceptions. Such request for registration on Form S-3 must cover securities the aggregate offering price of which, before payment of the underwriting discounts and commissions, equals or exceeds \$1,000,000. We will not be required to effect more than two registrations on Form S-3 pursuant to the amended and restated investor rights agreement.

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Table of Contents**Anti-Takeover Effects of Provisions of our Amended and Restated Certificate of Incorporation, our Amended and Restated Bylaws and Delaware Law**

Some provisions of Delaware law, our amended and restated certificate of incorporation and our amended and restated bylaws contain provisions that could make the following transactions more difficult: acquisition of us by means of a tender offer; acquisition of us by means of a proxy contest or otherwise; or removal of our incumbent officers and directors. It is possible that these provisions could make it more difficult to accomplish or could deter transactions that stockholders may otherwise consider to be in their best interest or in our best interests, including transactions that might result in a premium over the market price for our shares.

These provisions, summarized below, are expected to discourage coercive takeover practices and inadequate takeover bids. These provisions are also designed to encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure us outweigh the disadvantages of discouraging these proposals because negotiation of these proposals could result in an improvement of their terms.

Undesignated Preferred Stock

The ability to authorize undesignated preferred stock makes it possible for our board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring hostile takeovers or delaying changes in control or management of our company.

Stockholder Meetings

Our charter documents provide that a special meeting of stockholders may be called only by our board of directors, the chairman of our board of directors, our Chief Executive Officer or, in the absence of a Chief Executive Officer, our President.

Requirements for Advance Notification of Stockholder Nominations and Proposals

Our amended and restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee of the board of directors.

Elimination of Stockholder Action by Written Consent

Our amended and restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting.

Election and Removal of Directors

Our board of directors is divided into three classes. The directors in each class will serve for a three-year term, one class being elected each year by our stockholders. For more information on the classified board, see "Management—Board Composition." This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us, because it generally makes it more difficult for stockholders to replace a majority of the directors. Our charter documents provide that directors may be removed only for cause with the vote of holders of 66 2/3% of the voting power of all the then-outstanding shares of our voting stock.

Delaware Anti-Takeover Statute

We are subject to Section 203 of the Delaware General Corporation Law, which prohibits persons deemed "interested stockholders" from engaging in a "business combination" with a publicly-held Delaware corporation for three years following the date these persons become interested stockholders unless the business combination is, or the transaction in which the person became an interested stockholder was, approved in a prescribed manner or another prescribed exception applies. Generally, an "interested stockholder" is a person who, together with affiliates and associates, owns, or within three years prior to the determination of interested stockholder status did own, 15% or more of a corporation's voting stock. Generally, a "business combination" includes a merger, asset or stock sale, or other transaction resulting in a financial benefit to the interested stockholder. The existence of this provision may have an anti-takeover effect with respect to transactions not approved in advance by the board of directors, such as discouraging takeover attempts that might result in a premium over the market price of our common stock.

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Table of Contents**Amendment of our Amended and Restated Certificate of Incorporation or our Amended and Restated Bylaws**

The amendment of any of the above provisions in our amended and restated certificate of incorporation, except for the provision making it possible for our board of directors to issue preferred stock, or the amendment of any provision in our amended and restated bylaws (other than by action of the board of directors), would require approval by holders of at least 66 2/3% of our then outstanding voting stock.

The provisions of the Delaware General Corporation Law, our amended and restated certificate of incorporation and our amended and restated bylaws could have the effect of discouraging others from attempting hostile takeovers and, as a consequence, they may also inhibit temporary fluctuations in the market price of our common stock that often result from actual or rumored hostile takeover attempts. These provisions may also have the effect of preventing changes in our management. It is possible that these provisions could make it more difficult to accomplish transactions that stockholders may otherwise deem to be in their best interests.

Delaware as Sole and Exclusive Forum

Our amended and restated certificate of incorporation provide, that unless we consent in writing to an alternative forum, the Court of Chancery of the State of Delaware shall, to the fullest extent permitted by law, be the sole and exclusive forum for (i) any derivative action or proceeding brought on behalf of us, (ii) any action asserting a claim of breach of a fiduciary duty owed by, or otherwise wrongdoing by, any of our directors, officers or other employees to us or our stockholders, (iii) any action asserting a claim against us arising pursuant to any provision of the Delaware General Corporation Law or our amended and restated certificate of incorporation or amended and restated bylaws, (iv) any action to interpret, apply, enforce or determine the validity of our amended and restated certificate of incorporation or the bylaws, or (v) any action asserting a claim against us or any of our directors, officers or employees governed by the internal affairs doctrine.

Limitations of Liability and Indemnification Matters

For a discussion of liability and indemnification, please see "Management—Limitation on Liability and Indemnification Matters."

The NASDAQ Global Market Listing

We have applied to list our common stock on The NASDAQ Global Market under the trading symbol "AAVL."

Transfer Agent and Registrar

Upon the completion of this offering, the transfer agent and registrar for our common stock will be Wells Fargo Shareowner Services. The transfer agent and registrar's address is Wells Fargo Shareowner Services, Attn: Manager of Account Administration, 1110 Centre Pointe Curve, Suite 101, Mendota Heights, MN 55120-4101.

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Prior to this offering, there has been no public market for our common stock. Future sales of our common stock, including shares issued upon the exercise of outstanding options or warrants, in the public market after this offering, or the perception that those sales may occur, could cause the prevailing market price for our common stock to fall or impair our ability to raise equity capital in the future. As described below, only a limited number of shares of our common stock will be available for sale in the public market for a period of several months after completion of this offering due to contractual and legal restrictions on resale described below. Future sales of our common stock in the public market either before (to the extent permitted) or after restrictions lapse, or the perception that those sales may occur, could adversely affect the prevailing market price of common stock at such time and our ability to raise equity capital at a time and price we deem appropriate.

Sale of Restricted Shares

Based on the number of shares of our common stock outstanding as of March 31, 2014, upon the closing of this offering and the concurrent private placement to Regeneron and assuming (1) the conversion of our outstanding convertible preferred stock into common stock, assuming a purchase price of \$16.50 per share (the midpoint of the estimated range set forth on the cover page of this prospectus), (2) no exercise of the underwriters' option to purchase additional shares of common stock, (3) no exercise of outstanding options, (4) the exercise of all outstanding warrants and (5) the issuance of 606,060 shares of common stock offered by us in the concurrent private placement, assuming a purchase price of \$16.50 per share (the midpoint of the estimated range set forth on the cover page of this prospectus), we will have outstanding an aggregate of approximately 20,775,103 shares of common stock. Of these shares, all of the 5,400,000 shares of common stock to be sold in this offering, and any shares sold upon exercise of the underwriters' option to purchase additional shares, will be freely tradable in the public market without restriction or further registration under the Securities Act, unless the shares are held by any of our "affiliates" as such term is defined in Rule 144 of the Securities Act. All remaining shares of common stock held by existing stockholders immediately prior to the completion of this offering and any shares held by Regeneron (including those sold to it in the concurrent private placement) will be "restricted securities" as such term is defined in Rule 144. These restricted securities were issued and sold by us, or will be issued and sold by us, in private transactions and are eligible for public sale only if registered under the Securities Act or if they qualify for an exemption from registration under the Securities Act, including the exemptions provided by Rule 144 or Rule 701, which rules are summarized below.

As a result of the lock-up agreements referred to below and the provisions of Rule 144 and Rule 701 under the Securities Act, based on the number of shares of our common stock outstanding as of March 31, 2014, the number of shares of our common stock (excluding the shares sold in this offering) that will be available for sale in the public market, subject (1) to any waivers by the underwriters and/or our board of directors under the respective lock-up agreements and (2) with respect to shares held by directors, executive officers and other affiliates, the volume limitations under Rule 144 under the Securities Act, are as follows:

APPROXIMATE NUMBER OF SHARES	DATE AVAILABLE FOR SALE INTO PUBLIC MARKET
62,360 shares	90 days after the date of this prospectus
11,010,061 shares	180 days after the date of this prospectus
15,364,087 shares	One year after the date of this prospectus
15,364,087 shares	18-month anniversary of the date of this prospectus

Lock-Up Agreements

In connection with this offering, we, our officers, directors and holders of substantially all of our outstanding capital shares and other securities have agreed with the underwriters, subject to specified exceptions, not to directly or indirectly, and to use their best efforts to cause their immediate family members not to:

- sell, offer, contract or grant any option to sell (including any short sale), lend, pledge, transfer, establish or increase a "put equivalent position" or liquidate or decrease a "call equivalent position" within the meaning

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of Rule 16a-1(h) and Rule 16a-1(b), respectively, under the Exchange Act in, or otherwise dispose of any shares of our common stock, options or warrants to shares of our common stock, or securities or rights exchangeable or exercisable for or convertible into shares of our common stock;

- enter into any swap, hedge or similar arrangement or agreement that transfers, in whole or in part, the economic risk of ownership of shares of our common stock, or of options or warrants to shares of our common stock, or securities or rights exchangeable or exercisable for or convertible into shares of our common stock;
- make any demand for, or exercise any right with respect to, the registration under the Securities Act of 1933, as amended, of the offer and sale of any shares of our common stock, or of options or warrants to shares of our common stock, or securities or rights exchangeable or exercisable for or convertible into shares of our common stock, or cause to be filed a registration statement, prospectus or prospectus supplement (or an amendment or supplement thereto) with respect to any such registration; or
- publicly announce an intention to do any of the foregoing for a period of 180 days after the date of this prospectus without the prior written consent of Jefferies LLC and Cowen and Company, LLC.

Among other exceptions and subject to certain conditions, the foregoing restrictions will not apply to (i) certain transfers by gift, or by will or intestate succession, (ii) certain transfers or dispositions to any corporation, partnership or other entity all of the beneficial ownership interests of which are held by the locked up party or any family member, (iii) distributions by the locked up party to its partners, members or stockholders, (iv) the exercise of an option to purchase shares granted under any stock incentive plan or stock purchase plan of Avalanche, provided that the underlying shares shall continue to be subject to the restrictions set forth in the lock-up agreement, (v) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares, provided that such plan does not provide for any transfers of shares during the lock-up period and (vi) the transfer or disposition of shares acquired in the open market following this offering provided that no filing or other public announcement shall be required or made voluntarily in connection with such transfer or disposition during the lock-up period.

This restriction terminates after the close of trading of the common shares on and including the 180th day after the date of this prospectus.

Jefferies LLC and Cowen and Company, LLC may, in their sole discretion and at any time or from time to time before the termination of the 180-day period, without public notice, release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Rule 144

In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, a person (or persons whose shares are required to be aggregated) who is not deemed to have been one of our "affiliates" for purposes of Rule 144 at any time during the three months preceding a sale, and who has beneficially owned restricted securities within the meaning of Rule 144 for at least six months, including the holding period of any prior owner other than one of our "affiliates," is entitled to sell those shares in the public market (subject to the lock-up agreement referred to above, if applicable) without complying with the manner of sale, volume limitations or notice provisions of Rule 144, but subject to compliance with the public information requirements of Rule 144. If such a person has beneficially owned the sales proposed to be sold for at least one year, including the holding period of any prior owner other than "affiliates," then such person is entitled to sell such shares in the public market without complying with any of the requirements of Rule 144 (subject to the lock-up agreement referred to above, if applicable). In general, under Rule 144, as currently in effect, once we have been subject to the public company reporting requirements of the Exchange Act for at least 90 days, our "affiliates," as defined in Rule 144, who have beneficially owned the shares proposed to be sold for at least six months are entitled to sell in the public market, upon expiration of any applicable lock-up agreements and within any three-month period, a number of those shares of our common stock that does not exceed the greater of:

- 1% of the number of common shares then outstanding, which will equal approximately 207,751 shares of common stock immediately after this offering and the concurrent private placement (calculated on the basis of the

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assumptions described above and assuming no exercise of the underwriter's option to purchase additional shares and no exercise of outstanding options or warrants); or

- the average weekly trading volume of our common stock on The NASDAQ Global Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to such sale.

Such sales under Rule 144 by our "affiliates" or persons selling shares on behalf of our "affiliates" are also subject to certain manner of sale provisions, notice requirements and to the availability of current public information about us. Notwithstanding the availability of Rule 144, the holders of substantially all of our restricted securities have entered into lock-up agreements as referenced above and their restricted securities will become eligible for sale (subject to the above limitations under Rule 144) upon the expiration of the restrictions set forth in those agreements.

Rule 701

In general, under Rule 701 as currently in effect, any of our employees, directors, officers, consultants or advisors who acquired common stock from us in connection with a written compensatory stock or option plan or other written agreement in compliance with Rule 701 under the Securities Act before the effective date of the registration statement of which this prospectus is a part (to the extent such common stock is not subject to a lock-up agreement) is entitled to rely on Rule 701 to resell such shares beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act in reliance on Rule 144, but without compliance with the holding period requirements contained in Rule 144. Accordingly, subject to any applicable lock-up agreements, beginning 90 days after we become subject to the public company reporting requirements of the Exchange Act, under Rule 701 persons who are not our "affiliates," as defined in Rule 144, may resell those shares without complying with the minimum holding period or public information requirements of Rule 144, and persons who are our "affiliates" may resell those shares without compliance with Rule 144's minimum holding period requirements (subject to the terms of the lock-up agreement referred to above, if applicable).

Registration Rights

Based on the number of shares outstanding as of March 31, 2014, after the consummation of this offering and the concurrent private placement, the holders of approximately 11.9 million shares of our common stock, or their transferees, will, subject to any lock-up agreements they have entered into, be entitled to certain rights with respect to the registration of the offer and sale of those shares under the Securities Act. For a description of these registration rights, please see the section titled "Description of Capital Stock—Registration Rights." If the offer and sale of these shares are registered, they will be freely tradable without restriction under the Securities Act.

Equity Incentive Plans

We intend to file with the SEC a registration statement under the Securities Act covering the shares of common stock that we may issue upon exercise of outstanding options under our 2006 Plan and the shares of common stock that we may issue pursuant to future awards under our 2014 Plan and 2014 Employee Stock Purchase Plan. Such registration statement is expected to be filed and become effective as soon as practicable after the completion of this offering. Accordingly, shares registered under such registration statement will be available for sale in the open market following its effective date, subject to Rule 144 volume limitations and the lock-up agreements described above, if applicable.

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The following discussion is a summary of the material U.S. federal income tax consequences to Non-U.S. Holders (as defined below) of the purchase, ownership and disposition of our common stock issued pursuant to this offering but does not purport to be a complete analysis of all potential tax effects. The effects of other U.S. federal tax laws, such as estate and gift tax laws, and any applicable state, local or non-U.S. tax laws are not discussed. This discussion is based on the Code, Treasury Regulations promulgated thereunder, judicial decisions, and published rulings and administrative pronouncements of the IRS in each case in effect as of the date of this Registration Statement. These authorities may change or be subject to differing interpretations. Any such change or differing interpretation may be applied retroactively in a manner that could adversely affect a Non-U.S. Holder. We have not sought and will not seek any rulings from the IRS regarding the matters discussed below. There can be no assurance the IRS or a court will not take a contrary position to that discussed below regarding the tax consequences of the purchase, ownership and disposition of our common stock.

This discussion is limited to Non-U.S. Holders that hold our common stock as a "capital asset" within the meaning of Section 1221 of the Code (generally, property held for investment). This discussion does not address all U.S. federal income tax consequences relevant to a Non-U.S. Holder's particular circumstances, including the impact of the tax on net investment income imposed by Section 1411 of the Code. In addition, it does not address consequences relevant to Non-U.S. Holders subject to particular rules, including, without limitation:

- U.S. expatriates and former citizens or long-term residents of the United States;
- persons subject to the alternative minimum tax;
- persons holding our common stock as part of a hedge, straddle or other risk reduction strategy or as part of a conversion transaction or other integrated investment;
- banks, insurance companies and other financial institutions;
- brokers, dealers or traders in securities;
- "controlled foreign corporations," "passive foreign investment companies" and corporations that accumulate earnings to avoid U.S. federal income tax;
- partnerships or other entities or arrangements treated as partnerships for U.S. federal income tax purposes (and investors therein);
- tax-exempt organizations or governmental organizations;
- persons deemed to sell our common stock under the constructive sale provisions of the Code;
- persons who hold or receive our common stock pursuant to the exercise of any employee stock option or otherwise as compensation; and
- tax-qualified retirement plans.

If an entity treated as a partnership for U.S. federal income tax purposes holds our common stock, the tax treatment of a partner in the partnership will depend on the status of the partner, the activities of the partnership and certain determinations made at the partner level. Accordingly, partnerships holding our common stock and the partners in such partnerships should consult their tax advisors regarding the U.S. federal income tax consequences to them.

INVESTORS SHOULD CONSULT THEIR TAX ADVISORS WITH RESPECT TO THE APPLICATION OF THE U.S. FEDERAL INCOME TAX LAWS TO THEIR PARTICULAR SITUATIONS AS WELL AS ANY TAX CONSEQUENCES OF THE PURCHASE, OWNERSHIP AND DISPOSITION OF OUR COMMON STOCK ARISING UNDER THE U.S. FEDERAL ESTATE OR GIFT TAX LAWS OR UNDER THE LAWS OF ANY STATE, LOCAL OR NON-U.S. TAXING JURISDICTION OR UNDER ANY APPLICABLE INCOME TAX TREATY.

Definition of a Non-U.S. Holder

For purposes of this discussion, a "Non-U.S. Holder" is any beneficial owner of our common stock that is neither a "U.S. person" nor an entity treated as a partnership for U.S. federal income tax purposes. A U.S. person is any person that, for U.S. federal income tax purposes, is or is treated as any of the following:

- an individual who is a citizen or resident of the United States;
- a corporation created or organized under the laws of the United States, any state thereof or the District of Columbia;

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- an estate, the income of which is subject to U.S. federal income tax regardless of its source; or
- a trust that (1) is subject to the primary supervision of a U.S. court and the control of one or more "United States persons" (within the meaning of Section 7701(a)(30) of the Code) or (2) has a valid election in effect to be treated as a United States person for U.S. federal income tax purposes.

Distributions

As described in the section entitled "Dividend Policy," we do not anticipate paying any cash dividends in the foreseeable future. However, if we do make distributions of cash or property on our common stock, such distributions will constitute dividends for U.S. federal income tax purposes to the extent paid from our current or accumulated earnings and profits, as determined under U.S. federal income tax principles. Amounts not treated as dividends for U.S. federal income tax purposes will constitute a return of capital and first be applied against and reduce a Non-U.S. Holder's adjusted tax basis in its common stock, but not below zero. Any excess will be treated as capital gain and will be treated as described below under "—Sale or Other Taxable Disposition."

Subject to the discussion below on effectively connected income, dividends paid to a Non-U.S. Holder of our common stock will be subject to U.S. federal withholding tax at a rate of 30% of the gross amount of the dividends (or such lower rate specified by an applicable income tax treaty, provided the Non-U.S. Holder furnishes a valid IRS Form W-8BEN certifying qualification for the lower treaty rate). A Non-U.S. Holder that does not timely furnish the applicable withholding agent with the required certification, but that qualifies for a reduced treaty rate, may obtain a refund of any excess amounts withheld by timely filing an appropriate claim for refund with the IRS. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under any applicable income tax treaty.

If dividends paid to a Non-U.S. Holder are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such dividends are attributable), the Non-U.S. Holder will be exempt from the U.S. federal withholding tax described above. To claim the exemption, the Non-U.S. Holder must furnish to the applicable withholding agent a valid IRS Form W-8ECI, certifying that the dividends are effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States.

Any such effectively connected dividends will be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected dividends, as adjusted for certain items. Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Sale or Other Taxable Disposition

A Non-U.S. Holder will not be subject to U.S. federal income tax on any gain realized upon the sale or other taxable disposition of our common stock unless:

- the gain is effectively connected with the Non-U.S. Holder's conduct of a trade or business within the United States (and, if required by an applicable income tax treaty, the Non-U.S. Holder maintains a permanent establishment in the United States to which such gain is attributable);
- the Non-U.S. Holder is a nonresident alien individual present in the United States for 183 days or more during the taxable year of the disposition and certain other requirements are met; or
- our common stock constitutes a U.S. real property interest (USRPI) by reason of our status as a U.S. real property holding corporation (USRPHC) for U.S. federal income tax purposes.

Gain described in the first bullet point above will generally be subject to U.S. federal income tax on a net income basis at the regular graduated U.S. federal income tax rates. A Non-U.S. Holder that is a corporation also may be subject to a branch profits tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty) on such effectively connected gain, as adjusted for certain items.

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Gain described in the second bullet point above will be subject to U.S. federal income tax at a rate of 30% (or such lower rate specified by an applicable income tax treaty), which may be offset by U.S. source capital losses of the Non-U.S. Holder (even though the individual is not considered a resident of the United States), provided the Non-U.S. Holder has timely filed U.S. federal income tax returns with respect to such losses.

With respect to the third bullet point above, we believe we currently are not, and do not anticipate becoming, a USRPHC. Because the determination of whether we are a USRPHC depends, however, on the fair market value of our USRPIs relative to the fair market value of our non-U.S. real property interests and our other business assets, there can be no assurance we currently are not a USRPHC or will not become one in the future. Even if we are or were to become a USRPHC, gain arising from the sale or other taxable disposition by a Non-U.S. Holder of our common stock will not be subject to U.S. federal income tax if our common stock is "regularly traded," as defined by applicable Treasury Regulations, on an established securities market, and such Non-U.S. Holder owned, actually or constructively, 5% or less of our common stock throughout the shorter of the five-year period ending on the date of the sale or other taxable disposition or the Non-U.S. Holder's holding period.

Non-U.S. Holders should consult their tax advisors regarding any applicable tax treaties that may provide for different rules.

Information Reporting and Backup Withholding

Payments of dividends on our common stock will not be subject to backup withholding, provided the holder either certifies its non-U.S. status, such as by furnishing a valid IRS Form W-8BEN or W-8ECI, or otherwise establishes an exemption. However, information returns are required to be filed with the IRS in connection with any dividends on our common stock paid to the Non-U.S. Holder, regardless of whether any tax was actually withheld. Proceeds of the sale or other taxable disposition of our common stock within the United States or conducted through certain U.S.-related brokers generally will not be subject to backup withholding or information reporting, if the applicable withholding agent receives the certification described above, or the holder otherwise establishes an exemption. Proceeds of a disposition of our common stock conducted through a non-U.S. office of a non-U.S. broker generally will not be subject to backup withholding or information reporting.

Copies of information returns that are filed with the IRS may also be made available under the provisions of an applicable treaty or agreement to the tax authorities of the country in which the Non-U.S. Holder resides or is established.

Backup withholding is not an additional tax. Any amounts withheld under the backup withholding rules may be allowed as a refund or a credit against a Non-U.S. Holder's U.S. federal income tax liability, provided the required information is timely furnished to the IRS.

Additional Withholding Tax on Payments Made to Foreign Accounts

Withholding taxes may be imposed under Sections 1471 to 1474 of the Code (such Sections commonly referred to as the Foreign Account Tax Compliance Act (FATCA)) on certain types of payments made to non-U.S. financial institutions and certain other non-U.S. entities. Specifically, a 30% withholding tax may be imposed on dividends paid on, or gross proceeds from the sale or other disposition of, our common stock paid to a "foreign financial institution" or a "non-financial foreign entity" (each as defined in the Code), unless (1) the foreign financial institution undertakes certain diligence and reporting obligations, (2) the non-financial foreign entity either certifies it does not have any "substantial United States owners" (as defined in the Code) or furnishes identifying information regarding each substantial United States owner, or (3) the foreign financial institution or non-financial foreign entity otherwise qualifies for an exemption from these rules. If the payee is a foreign financial institution and is subject to the diligence and reporting requirements in (1) above, it must enter into an agreement with the U.S. Department of the Treasury requiring, among other things, that it undertake to identify accounts held by certain "specified United States persons" or "United States-owned foreign entities" (each as defined in the Code), annually report certain information about such accounts, and withhold 30% on certain payments to non-compliant foreign financial institutions and certain other account holders. Foreign financial institutions located in jurisdictions that have an intergovernmental agreement with the United States governing FATCA may be subject to different rules.

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Under the applicable Treasury Regulations and IRS guidance, withholding under FATCA generally will apply to payments of dividends on our common stock made on or after July 1, 2014, and to payments of gross proceeds from the sale or other disposition of such stock on or after January 1, 2017.

Prospective investors should consult their tax advisors regarding the potential application of withholding under FATCA to their investment in our common stock.

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Table of Contents**UNDERWRITING**

Subject to the terms and conditions set forth in the underwriting agreement, dated _____, 2014, between us, Jefferies LLC and Cowen and Company, LLC, as the representatives of the underwriters named below and, together with Piper Jaffray & Co., the joint book-running managers of this offering, we have agreed to sell to the underwriters, and each of the underwriters has agreed, severally and not jointly, to purchase from us, the respective number of shares of common stock shown opposite its name below:

<u>UNDERWRITER</u>	<u>NUMBER OF SHARES</u>
Jefferies LLC	
Cowen and Company, LLC	
Piper Jaffray & Co.	
William Blair & Company, L.L.C.	
Total	<u>5,400,000</u>

The underwriting agreement provides that the obligations of the several underwriters are subject to certain conditions precedent such as the receipt by the underwriters of officers' certificates and legal opinions and approval of certain legal matters by their counsel. The underwriting agreement provides that the underwriters will purchase all of the shares of common stock if any of them are purchased. If an underwriter defaults, the underwriting agreement provides that the purchase commitments of the nondefaulting underwriters may be increased or the underwriting agreement may be terminated. We have agreed to indemnify the underwriters and certain of their controlling persons against certain liabilities, including liabilities under the Securities Act, and to contribute to payments that the underwriters may be required to make in respect of those liabilities.

The underwriters have advised us that, following the completion of this offering, they currently intend to make a market in the common stock as permitted by applicable laws and regulations. However, the underwriters are not obligated to do so, and the underwriters may discontinue any market-making activities at any time without notice in their sole discretion. Accordingly, no assurance can be given as to the liquidity of the trading market for the common stock, that you will be able to sell any of the common stock held by you at a particular time or that the prices that you receive when you sell will be favorable.

Certain of our existing investors have indicated an interest in purchasing an aggregate of approximately \$30.0 million of shares of the common stock in this offering on the same terms as those offered to the public. However, indications of interest are not binding agreements or commitments to purchase and any of these entities may determine to purchase more, fewer or no shares in this offering.

The underwriters are offering the shares of common stock subject to their acceptance of the shares of common stock from us and subject to prior sale. The underwriters reserve the right to withdraw, cancel or modify offers to the public and to reject orders in whole or in part.

Commission and Expenses

The underwriters have advised us that they propose to offer the shares of common stock to the public at the initial public offering price set forth on the cover page of this prospectus and to certain dealers, which may include the underwriters, at that price less a concession not in excess of \$ _____ per share of common stock. The underwriters may allow, and certain dealers may reallow, a discount from the concession not in excess of \$ _____ per share of common stock to certain brokers and dealers. After the offering, the initial public offering price, concession and reallowance to dealers may be reduced by the representatives. No such reduction will change the amount of proceeds to be received by us as set forth on the cover page of this prospectus.

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The following table shows the public offering price, the underwriting discounts and commissions that we are to pay the underwriters and the proceeds, before expenses, to us in connection with this offering. Such amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares.

	PER SHARE		TOTAL	
	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES	WITHOUT OPTION TO PURCHASE ADDITIONAL SHARES	WITH OPTION TO PURCHASE ADDITIONAL SHARES
Public offering price	\$	\$	\$	\$
Underwriting discounts and commissions paid by us	\$	\$	\$	\$
Proceeds to us, before expenses	\$	\$	\$	\$

We estimate expenses payable by us in connection with this offering, other than the underwriting discounts and commissions referred to above, will be approximately \$2.3 million. We have agreed to reimburse the underwriters up to \$40,000 for their FINRA counsel fee. In accordance with FINRA Rule 5110, this reimbursed fee is deemed underwriting compensation for this offering.

Determination of Offering Price

Prior to this offering, there has not been a public market for our common stock. Consequently, the initial public offering price for our common stock will be determined by negotiations between us and the representatives. Among the factors to be considered in these negotiations will be prevailing market conditions, our financial information, market valuations of other companies that we and the underwriters believe to be comparable to us, estimates of our business potential, the present state of our development and other factors deemed relevant.

We offer no assurances that the initial public offering price will correspond to the price at which the common stock will trade in the public market subsequent to the offering or that an active trading market for the common stock will develop and continue after the offering.

Listing

We have applied to have our common stock listed on The NASDAQ Global Market under the trading symbol "AAVL."

Stamp Taxes

If you purchase shares of common stock offered in this prospectus, you may be required to pay stamp taxes and other charges under the laws and practices of the country of purchase, in addition to the offering price listed on the cover page of this prospectus.

Option to Purchase Additional Shares

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase, from time to time, in whole or in part, up to an aggregate of 810,000 shares from us at the public offering price set forth on the cover page of this prospectus, less underwriting discounts and commissions. If the underwriters exercise this option, each underwriter will be obligated, subject to specified conditions, to purchase a number of additional shares proportionate to that underwriter's initial purchase commitment as indicated in the table above. This option may be exercised only if the underwriters sell more shares than the total number set forth on the cover page of this prospectus.

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Table of Contents**No Sales of Similar Securities**

We, our officers, directors and holders of all or substantially all our outstanding capital stock and other securities have agreed, subject to specified exceptions, not to directly or indirectly:

- sell, offer, contract or grant any option to sell (including any short sale), lend, pledge, transfer, establish or increase a "put equivalent position" or liquidate or decrease a "call equivalent position" within the meaning of Rule 16a-1(h) and Rule 16a-1(b), respectively, under the Exchange Act in, or otherwise dispose of any shares of our common stock, options or warrants to shares of our common stock, or securities or rights exchangeable or exercisable for or convertible into shares of our common stock;
- enter into any swap, hedge or similar arrangement or agreement that transfers, in whole or in part, the economic risk of ownership of shares of our common stock, or of options or warrants to shares of our common stock, or securities or rights exchangeable or exercisable for or convertible into shares of our common stock;
- make any demand for, or exercise any right with respect to, the registration under the Securities Act of 1933, as amended, of the offer and sale of any shares of our common stock, or of options or warrants to shares of our common stock, or securities or rights exchangeable or exercisable for or convertible into shares of our common stock, or cause to be filed a registration statement, prospectus or prospectus supplement (or an amendment or supplement thereto) with respect to any such registration; or
- publicly announce an intention to do any of the foregoing for a period of 180 days after the date of this prospectus without the prior written consent of Jefferies LLC and Cowen and Company, LLC.

Among other exceptions and subject to certain conditions, the foregoing restrictions will not apply to (i) certain transfers by gift, or by will or intestate succession, (ii) certain transfers or dispositions to any corporation, partnership or other entity all of the beneficial ownership interests of which are held by the locked up party or any family member, (iii) distributions by the locked up party to its partners, members or stockholders, (iv) the exercise of an option to purchase shares granted under any stock incentive plan or stock purchase plan of Avalanche, provided that the underlying shares shall continue to be subject to the restrictions set forth in the lock-up agreement, (v) the establishment of a trading plan pursuant to Rule 10b5-1 under the Exchange Act for the transfer of shares, provided that such plan does not provide for any transfers of shares during the lock-up period and (vi) the transfer or disposition of shares acquired on the open market following this offering provided that no filing or other public announcement shall be required or made voluntarily in connection with such transfer or disposition during the lock-up period.

This restriction terminates after the close of trading of the common stock on and including the 180th day after the date of this prospectus.

Jefferies LLC and Cowen and Company, LLC may, in their sole discretion and at any time or from time to time before the termination of the 180-day period, release all or any portion of the securities subject to lock-up agreements. There are no existing agreements between the underwriters and any of our shareholders who will execute a lock-up agreement, providing consent to the sale of shares prior to the expiration of the lock-up period.

Stabilization

The underwriters have advised us that, pursuant to Regulation M under the Exchange Act, certain persons participating in the offering may engage in short sale transactions, stabilizing transactions, syndicate covering transactions or the imposition of penalty bids in connection with this offering. These activities may have the effect of stabilizing or maintaining the market price of the common stock at a level above that which might otherwise prevail in the open market. Establishing short sales positions may involve either "covered" short sales or "naked" short sales.

"Covered" short sales are sales made in an amount not greater than the underwriters' option to purchase additional shares of our common stock in this offering. The underwriters may close out any covered short position by either exercising their option to purchase additional shares of our common stock or purchasing shares of our common stock in the open market. In determining the source of shares to close out the covered short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the option to purchase additional shares.

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"Naked" short sales are sales in excess of the option to purchase additional shares of our common stock. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares of our common stock in the open market after pricing that could adversely affect investors who purchase in this offering.

A stabilizing bid is a bid for the purchase of shares of common stock on behalf of the underwriters for the purpose of fixing or maintaining the price of the common stock. A syndicate covering transaction is the bid for or the purchase of shares of common stock on behalf of the underwriters to reduce a short position incurred by the underwriters in connection with the offering. Similar to other purchase transactions, the underwriter's purchases to cover the syndicate short sales may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of our common stock. As a result, the price of our common stock may be higher than the price that might otherwise exist in the open market. A penalty bid is an arrangement permitting the underwriters to reclaim the selling concession otherwise accruing to a syndicate member in connection with the offering if the common stock originally sold by such syndicate member are purchased in a syndicate covering transaction and therefore have not been effectively placed by such syndicate member.

Neither we, nor any of the underwriters make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of our common stock. The underwriters are not obligated to engage in these activities and, if commenced, any of the activities may be discontinued at any time.

The underwriters may also engage in passive market making transactions in our common stock on The NASDAQ Global Market in accordance with Rule 103 of Regulation M during a period before the commencement of offers or sales of shares of our common stock in this offering and extending through the completion of distribution. A passive market maker must display its bid at a price not in excess of the highest independent bid of that security. However, if all independent bids are lowered below the passive market maker's bid, that bid must then be lowered when specified purchase limits are exceeded.

Electronic Distribution

A prospectus in electronic format may be made available by e-mail or on the web sites or through online services maintained by one or more of the underwriters or their affiliates. In those cases, prospective investors may view offering terms online and may be allowed to place orders online. The underwriters may agree with us to allocate a specific number of shares of common stock for sale to online brokerage account holders. Any such allocation for online distributions will be made by the underwriters on the same basis as other allocations. Other than the prospectus in electronic format, the information on the underwriters' web sites and any information contained in any other web site maintained by any of the underwriters is not part of this prospectus, has not been approved and/or endorsed by us or the underwriters and should not be relied upon by investors.

Other Activities and Relationships

The underwriters and certain of their affiliates are full service financial institutions engaged in various activities, which may include securities trading, commercial and investment banking, financial advisory, investment management, investment research, principal investment, hedging, financing and brokerage activities. The underwriters and certain of their affiliates have, from time to time, performed, and may in the future perform, various commercial and investment banking and financial advisory services for us and our affiliates, for which they received or will receive customary fees and expenses.

In the ordinary course of their various business activities, the underwriters and certain of their affiliates may make or hold a broad array of investments and actively trade debt and equity securities (or related derivative securities) and financial instruments (including bank loans) for their own account and for the accounts of their customers, and such investment and securities activities may involve securities and/or instruments issued by us and our affiliates. If the underwriters or their respective affiliates have a lending relationship with us, they routinely hedge their credit exposure to us consistent with their customary risk management policies. The underwriters and their respective affiliates may hedge such exposure by entering into transactions which consist of either the purchase of credit default swaps or the creation of short positions in our securities or the securities of our affiliates, including

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potentially the common stock offered hereby. Any such short positions could adversely affect future trading prices of the common stock offered hereby. The underwriters and certain of their respective affiliates may also communicate independent investment recommendations, market color or trading ideas and/or publish or express independent research views in respect of such securities or instruments and may at any time hold, or recommend to clients that they acquire, long and/or short positions in such securities and instruments.

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NOTICE TO INVESTORS

Australia

This prospectus is not a disclosure document for the purposes of Australia's Corporations Act 2001 (Cth) of Australia (Corporations Act), has not been lodged with the Australian Securities & Investments Commission and is only directed to the categories of exempt persons set out below. Accordingly, if you receive this prospectus in Australia:

You confirm and warrant that you are either:

- a "sophisticated investor" under section 708(8)(a) or (b) of the Corporations Act;
- a "sophisticated investor" under section 708(8)(c) or (d) of the Corporations Act and that you have provided an accountant's certificate to the company which complies with the requirements of section 708(8)(c)(i) or (ii) of the Corporations Act and related regulations before the offer has been made; or
- a "professional investor" within the meaning of section 708(11)(a) or (b) of the Corporations Act.

To the extent that you are unable to confirm or warrant that you are an exempt sophisticated investor or professional investor under the Corporations Act any offer made to you under this prospectus is void and incapable of acceptance.

You warrant and agree that you will not offer any of the shares issued to you pursuant to this prospectus for resale in Australia within 12 months of those shares being issued unless any such resale offer is exempt from the requirement to issue a disclosure document under section 708 of the Corporations Act.

European Economic Area

In relation to each member state of the European Economic Area which has implemented the Prospectus Directive, each referred to herein as a Relevant Member State, with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State, referred to herein as the Relevant Implementation Date, no offer of any securities which are the subject of the offering contemplated by this prospectus has been or will be made to the public in that Relevant Member State other than any offer where a prospectus has been or will be published in relation to such securities that has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the relevant competent authority in that Relevant Member State in accordance with the Prospectus Directive, except that with effect from and including the Relevant Implementation Date, an offer of such securities may be made to the public in that Relevant Member State:

- to any legal entity which is a "qualified investor" as defined in the Prospectus Directive;
- to fewer than 100 or, if the Relevant Member State has implemented the relevant provision of the 2010 PD Amending Directive, 150, natural or legal persons (other than qualified investors as defined in the Prospectus Directive), as permitted under the Prospectus Directive, subject to obtaining the prior consent of the representatives of the underwriters for any such offer; or
- in any other circumstances falling within Article 3(2) of the Prospectus Directive,

provided that no such offer of securities shall require the Company or any of the underwriters to publish a prospectus pursuant to Article 3 of the Prospectus Directive or supplement a prospectus pursuant to Article 16 of the Prospectus Directive.

For the purposes of this provision, the expression an "offer to the public" in relation to any securities in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of the offer and the securities to be offered so as to enable an investor to decide to purchase or subscribe the securities, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression "Prospectus Directive" means Directive 2003/71/EC (and amendments thereto, including the 2010 PD Amending Directive, to the extent implemented in the Relevant Member State), and includes any relevant implementing measure in the Relevant Member State and the expression "2010 PD Amending Directive" means Directive 2010/73/EU.

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No securities have been offered or sold, and no securities may be offered or sold, in Hong Kong, by means of any document, other than to persons whose ordinary business is to buy or sell shares or debentures, whether as principal or agent; or to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance; or in other circumstances which do not result in the document being a "prospectus" as defined in the Companies Ordinance (Cap. 32) of Hong Kong or which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap.32) of Hong Kong. No document, invitation or advertisement relating to the securities has been issued or may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public of Hong Kong (except if permitted under the securities laws of Hong Kong) other than with respect to securities which are or are intended to be disposed of only to persons outside Hong Kong or only to "professional investors" as defined in the Securities and Futures Ordinance (Cap. 571) of Hong Kong and any rules made under that Ordinance.

This prospectus has not been registered with the Registrar of Companies in Hong Kong. Accordingly, this prospectus may not be issued, circulated or distributed in Hong Kong, and the securities may not be offered for subscription to members of the public in Hong Kong. Each person acquiring the securities will be required, and is deemed by the acquisition of the securities, to confirm that he is aware of the restriction on offers of the securities described in this prospectus and the relevant offering documents and that he is not acquiring, and has not been offered any securities in circumstances that contravene any such restrictions.

Japan

The offering has not been and will not be registered under the Financial Instruments and Exchange Law of Japan (Law No. 25 of 1948 of Japan, as amended) (FIEL), and the Initial Purchaser will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means, unless otherwise provided herein, any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the FIEL and any other applicable laws, regulations and ministerial guidelines of Japan.

Singapore

This prospectus has not been and will not be lodged or registered with the Monetary Authority of Singapore. Accordingly, this prospectus and any other document or material in connection with the offer or sale, or the invitation for subscription or purchase of the securities may not be issued, circulated or distributed, nor may the securities be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to the public or any member of the public in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (SFA), (ii) to a relevant person as defined under Section 275(2), or any person pursuant to Section 275(1A) of the SFA, and in accordance with the conditions, specified in Section 275 of the SFA, or (iii) otherwise pursuant to, and in accordance with the conditions of any other applicable provision of the SFA.

Where the securities are subscribed or purchased under Section 275 of the SFA by a relevant person which is:

- a corporation (which is not an accredited investor as defined under Section 4A of the SFA) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or
- a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary is an accredited investor,

shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for six months after that corporation or that trust has acquired the Offer Shares under Section 275 of the SFA except:

- to an institutional investor under Section 274 of the SFA or to a relevant person defined in Section 275(2) of the SFA, or to any person pursuant to an offer that is made on terms that such shares, debentures and

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units of shares and debentures of that corporation or such rights and interest in that trust are acquired at a consideration of not less than \$200,000 (or its equivalent in a foreign currency) for each transaction, whether such amount is to be paid for in cash or by exchange of securities or other assets, and further for corporations, in accordance with the conditions, specified in Section 275 of the SFA;

- where no consideration is given for the transfer; or
- where the transfer is by operation of law.

Switzerland

The securities may not be publicly offered in Switzerland and will not be listed on the SIX Swiss Exchange (SIX) or on any other stock exchange or regulated trading facility in Switzerland. This prospectus has been prepared without regard to the disclosure standards for issuance prospectuses under art. 652a or art. 1156 of the Swiss Code of Obligations or the disclosure standards for listing prospectuses under art. 27 ff. of the SIX Listing Rules or the listing rules of any other stock exchange or regulated trading facility in Switzerland. Neither this prospectus nor any other offering or marketing material relating to the securities or the offering may be publicly distributed or otherwise made publicly available in Switzerland.

Neither this prospectus nor any other offering or marketing material relating to the offering, the Company or the securities have been or will be filed with or approved by any Swiss regulatory authority. In particular, this prospectus will not be filed with, and the offer of securities will not be supervised by, the Swiss Financial Market Supervisory Authority (FINMA), and the offer of securities has not been and will not be authorized under the Swiss Federal Act on Collective Investment Schemes (CISA). The investor protection afforded to acquirers of interests in collective investment schemes under the CISA does not extend to acquirers of securities.

United Kingdom

This prospectus is only being distributed to, and is only directed at, persons in the United Kingdom that are qualified investors within the meaning of Article 2(1)(e) of the Prospectus Directive that are also (i) investment professionals falling within Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (Order) and/or (ii) high net worth entities falling within Article 49(2)(a) to (d) of the Order and other persons to whom it may lawfully be communicated. Each such person is referred to herein as a Relevant Person.

This prospectus and its contents are confidential and should not be distributed, published or reproduced (in whole or in part) or disclosed by recipients to any other persons in the United Kingdom. Any person in the United Kingdom that is not a Relevant Person should not act or rely on this document or any of its contents.

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LEGAL MATTERS

The validity of the issuance of our Common Stock offered in this prospectus will be passed upon for us by Latham & Watkins LLP, Menlo Park, California. Covington & Burling LLP, New York, New York is counsel to the underwriters in this offering. Latham & Watkins LLP and certain attorneys and investment funds affiliated with the firm collectively own an aggregate of 6,640 shares of our convertible preferred stock which will be converted into an aggregate of 6,640 shares of common stock immediately prior to the completion of this offering.

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EXPERTS

The consolidated financial statements included in this prospectus have been audited by Deloitte & Touche LLP, an independent registered public accounting firm, as stated in their report appearing herein (which report expresses an unqualified opinion on the consolidated financial statements and includes an explanatory paragraph which refers to the Company being in the development stage as of December 31, 2013). Such consolidated financial statements have been so included in reliance upon the report of such firm given upon their authority as experts in accounting and auditing.

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[Table of Contents](#)**WHERE YOU CAN FIND MORE INFORMATION**

We have filed with the SEC a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus, which constitutes a part of the registration statement, does not contain all of the information set forth in the registration statement or the exhibits and schedules filed therewith. For further information with respect to Avalanche Biotechnologies, Inc. and the common stock offered hereby, reference is made to the registration statement and the exhibits and schedules filed therewith. Statements contained in this prospectus regarding the contents of any contract or any other document that is filed as an exhibit to the registration statement are not necessarily complete, and each such statement is qualified in all respects by reference to the full text of such contract or other document filed as an exhibit to the registration statement. A copy of the registration statement and the exhibits and schedules filed therewith may be inspected without charge at the public reference room maintained by the SEC, located at 100 F Street N.E., Room 1580, Washington, D.C. 20549, and copies of all or any part of the registration statement may be obtained from such offices upon the payment of the fees prescribed by the SEC. Please call the SEC at 1-800-SEC-0330 for further information about the public reference room. The SEC also maintains a website that contains reports, proxy and information statements and other information regarding registrants that file electronically with the SEC. The address is www.sec.gov.

Upon completion of this offering, we will become subject to the information and periodic reporting requirements of the Exchange Act and, in accordance therewith, will file periodic reports, proxy statements and other information with the SEC. Such periodic reports, proxy statements and other information will be available for inspection and copying at the public reference room and website of the SEC referred to above. We maintain a website at www.avalanchebiotech.com. You may access our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act with the SEC free of charge at our website as soon as reasonably practicable after such material is electronically filed with, or furnished to, the SEC. The reference to our website address does not constitute incorporation by reference of the information contained on our website, and you should not consider the contents of our website in making an investment decision with respect to our common stock.

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AVALANCHE BIOTECHNOLOGIES, INC.
(a development stage company)

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of
Avalanche Biotechnologies, Inc.
(a development stage company)

We have audited the accompanying consolidated balance sheets of Avalanche Biotechnologies, Inc. and its subsidiary (collectively the "Company") (a development stage company) as of December 31, 2013 and 2012, and the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' deficit, and cash flows for the years then ended, and for the period from July 17, 2006 (date of inception) to December 31, 2013. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. The Company is not required to have, nor were we engaged to perform, an audit of their internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of Avalanche Biotechnologies, Inc. and its subsidiary as of December 31, 2013 and 2012, and the results of their operations and their cash flows for the years then ended, and for the period from July 17, 2006 (date of inception) to December 31, 2013, in conformity with accounting principles generally accepted in the United States of America.

As discussed in Note 1, the Company has devoted its efforts principally to research and development activities, and is in the development stage as of December 31, 2013. The Company's success is dependent upon its ability to successfully develop, commercialize and market its products, earn revenue, obtain additional capital when needed, and, ultimately, to achieve profitable operations.

/s/ Deloitte & Touche LLP

San Jose, California
May 30, 2014

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AVALANCHE BIOTECHNOLOGIES, INC.
(a development stage company)
CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share data)

	<u>DECEMBER 31,</u>		<u>MARCH 31,</u>	<u>PRO FORMA</u>
	<u>2012</u>	<u>2013</u>	<u>2014</u>	<u>MARCH 31,</u>
			<u>(unaudited)</u>	<u>2014</u>
				<u>(unaudited)</u>
ASSETS				
Current assets:				
Cash	\$ 357	\$ 564	\$ 169	\$ 50,679
Accounts receivable	1	8	233	233
Prepaid expenses and other current assets	24	250	354	354
Total current assets	382	822	756	51,266
Property and equipment, net	4	69	107	107
Deposit and other assets	—	194	240	240
Total assets	<u>\$ 386</u>	<u>\$ 1,085</u>	<u>\$ 1,103</u>	<u>\$ 51,613</u>
LIABILITIES, CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)				
Current liabilities:				
Accounts payable	\$ 522	\$ 769	\$ 946	\$ 946
Accrued expenses and other current liabilities	317	393	662	662
Total current liabilities	839	1,162	1,608	1,608
Long-term liabilities:				
Related-party convertible notes	485	—	14	14
Common stock warrant liability	5	42	—	—
Convertible preferred stock warrant liability	36	91	129	—
Embedded derivative liability	18	—	—	—
Deferred rent	—	8	77	77
Total liabilities	<u>1,383</u>	<u>1,303</u>	<u>1,828</u>	<u>1,699</u>
Commitments and contingencies (Note 7)				
Convertible preferred stock (Note 9)				
Series A convertible preferred stock, par value \$0.0001 per share—2,123,681 and 4,233,295 and 4,233,295 shares authorized at December 31, 2012, December 31, 2013 and March 31, 2014 (unaudited), respectively; 1,789,618 and 3,899,232 and 3,899,232 shares issued and outstanding at December 31, 2012 and December 31, 2013 and March 31, 2014 (unaudited), respectively; (liquidation preference of \$2,595 and \$5,654 and \$5,654 at December 31, 2012 and December 31, 2013 and March 31, 2014 (unaudited), respectively); no issued and outstanding, pro forma (unaudited)	2,471	7,992	7,992	—
Stockholders' deficit:				
Common stock, par value \$0.0001 per share—8,068,951 and 15,000,000 and 15,000,000 shares authorized at December 31, 2012, December 31, 2013 and March 31, 2014 (unaudited), respectively; 3,672,885 shares issued and outstanding at December 31, 2012, December 31, 2013 and March 31, 2014 (unaudited), respectively; 14,769,043 issued and outstanding, pro forma (unaudited)	—	—	—	1
Additional paid-in capital	117	632	1,788	63,082
Accumulated other comprehensive income	8	27	27	27
Deficit accumulated during the development stage	(3,593)	(8,869)	(10,532)	(13,196)
Total stockholders' equity (deficit)	<u>(3,468)</u>	<u>(8,210)</u>	<u>(8,717)</u>	<u>49,914</u>
Total liabilities, convertible preferred stock and stockholders' equity (deficit)	<u>\$ 386</u>	<u>\$ 1,085</u>	<u>\$ 1,103</u>	<u>\$ 51,613</u>

See accompanying notes to consolidated financial statements.

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AVALANCHE BIOTECHNOLOGIES, INC.
(a development stage company)

CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(In thousands, except share and per share data)

	YEARS ENDED DECEMBER 31,		PERIOD FROM JULY 17, 2006 (DATE OF INCEPTION) TO DECEMBER 31, 2013	THREE MONTHS ENDED MARCH 31,		PERIOD FROM JULY 17, 2006 (DATE OF INCEPTION) TO MARCH 31, 2014
	2012	2013	2013	2013 (unaudited)	2014 (unaudited)	(unaudited)
License revenue	\$ —	\$ —	\$ —	\$ —	\$ 30	\$ 30
Government grant revenue	30	480	510	300	—	510
Total revenue	30	480	510	300	30	540
Operating expenses:						
Research and development	1,310	2,151	4,636	201	910	5,546
General and administrative	536	1,783	2,905	141	726	3,631
Total operating expenses	1,846	3,934	7,541	342	1,636	9,177
Operating loss	(1,816)	(3,454)	(7,031)	(42)	(1,606)	(8,637)
Other (expense) income:						
Interest expense	(8)	(73)	(100)	(13)	(14)	(114)
Other income (expense), net	7	(96)	(91)	6	(43)	(134)
Change in fair value of embedded derivative	6	18	24	—	—	24
Loss on extinguishment of related-party convertible notes	—	(1,671)	(1,671)	—	—	(1,671)
Total other (expense) income, net	5	(1,822)	(1,838)	(7)	(57)	(1,895)
Net loss	(1,811)	(5,276)	(8,869)	(49)	(1,663)	(10,532)
Other comprehensive income (loss):						
Foreign currency translation adjustment	8	19	27	—	—	27
Comprehensive loss	\$ (1,803)	\$ (5,257)	\$ (8,842)	\$ (49)	\$ (1,663)	\$ (10,505)
Net loss per share attributable to common stockholders— basic and diluted	\$ (0.50)	\$ (1.44)		\$ (0.01)	\$ (0.45)	
Weighted-average common shares outstanding—basic and diluted	3,642,503	3,672,885		3,672,885	3,672,885	
Pro forma net loss per share attributable to common stockholders—basic and diluted		\$ (0.74)			\$ (0.11)	
Pro forma weighted-average common shares outstanding—basic and diluted		6,889,774			14,741,705	

See accompanying notes to consolidated financial statements.

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AVALANCHE BIOTECHNOLOGIES, INC.
(a development stage company)
**CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK
AND STOCKHOLDERS' DEFICIT**
(In thousands except share and per share data)

	SERIES A CONVERTIBLE PREFERRED STOCK \$0.0001 PAR VALUE		COMMON STOCK \$0.0001 PAR VALUE		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED OTHER COMPREHENSIVE INCOME	DEFICIT ACCUMULATED DURING THE DEVELOPMENT STAGE	TOTAL STOCKHOLDERS' DEFICIT
	SHARES	AMOUNT	SHARES	AMOUNT				
DATE OF INCEPTION— JULY 17, 2006	—	\$ —	—	\$ —	—	\$ —	—	\$ —
Issuance of common stock for cash	—	—	210,000	—	—	—	—	—
Vesting of common stock related to purchase of unvested restricted stock	—	—	4,451,042	—	—	—	—	—
Issuance of common stock to consultants for services provided	—	—	41,010	—	—	—	—	—
Repurchase of founders shares in July and August 2010	—	—	(1,200,000)	—	—	—	—	—
Common stock issued upon exercise of stock options	—	—	71,875	—	—	—	—	—
Conversion of convertible notes and accrued interest into Series A convertible preferred stock at \$1.45 per share in September 2010, net of amounts allocated to detachable warrants of \$54	149,979	164	—	—	—	—	—	—
Issuance of Series A convertible preferred stock in September and December 2010 for cash, net of issuance costs of \$71	1,536,205	2,157	—	—	—	—	—	—
Issuance of Series A convertible preferred stock in April 2011 for cash	103,434	150	—	—	—	—	—	—
Issuance of common stock warrants in partial consideration for intellectual property	—	—	—	—	13	—	—	13
Stock-based compensation expense	—	—	—	—	25	—	—	25
Net loss	—	—	—	—	—	—	(1,782)	(1,782)
BALANCE—								

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DECEMBER 31, 2011	1,789,618	2,471	3,573,927	—	38	—	(1,782)	(1,744)
Vesting of common stock related to purchase of unvested restricted stock	—	—	98,958	—	—	—	—	—
Issuance of common stock warrants in partial consideration for intellectual property	—	—	—	—	3	—	—	3
Stock-based compensation expense	—	—	—	—	76	—	—	76
Foreign currency translation adjustment	—	—	—	—	—	8	—	8
Net loss	—	—	—	—	—	—	(1,811)	(1,811)
BALANCE—								
DECEMBER 31, 2012	1,789,618	2,471	3,672,885	—	117	8	(3,593)	(3,468)

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AVALANCHE BIOTECHNOLOGIES, INC.
(a development stage company)
**CONSOLIDATED STATEMENTS OF CONVERTIBLE PREFERRED STOCK
AND STOCKHOLDERS' DEFICIT (continued)**
(In thousands except share and per share data)

	SERIES A CONVERTIBLE PREFERRED STOCK \$0.0001 PAR VALUE		COMMON STOCK \$0.0001 PAR VALUE		ADDITIONAL PAID-IN CAPITAL	ACCUMULATED OTHER COMPREHENSIVE INCOME	DEFICIT ACCUMULATED DURING THE DEVELOPMENT STAGE	TOTAL STOCKHOLDERS' DEFICIT
	SHARES	AMOUNT	SHARES	AMOUNT				
BALANCE— DECEMBER 31, 2012	1,789,618	2,471	3,672,885	—	117	8	(3,593)	(3,468)
Conversion of the related- party convertible notes and accrued interest into Series A convertible preferred stock in November 2013	1,419,959	3,730	—	—	—	—	—	—
Issuance of Series A convertible preferred stock in November 2013 for cash, net of issuance costs of \$20	689,655	1,791	—	—	—	—	—	—
Stock-based compensation expense	—	—	—	—	515	—	—	515
Foreign currency translation adjustment	—	—	—	—	—	19	—	19
Net loss	—	—	—	—	—	—	(5,276)	(5,276)
BALANCE— DECEMBER 31, 2013	3,899,232	7,992	3,672,885	—	632	27	(8,869)	(8,210)
Beneficial conversion feature in related- party convertible notes (unaudited)	—	—	—	—	1,000	—	—	1,000
Stock-based compensation expense (unaudited)	—	—	—	—	115	—	—	115
Issuance of common stock warrant in consideration for services								

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(unaudited)	—	—	—	—	41	—	—	41
Net loss								
(unaudited)	—	—	—	—	—	—	(1,663)	(1,663)
BALANCE—								
MARCH								
31, 2014								
(unaudited)	<u>3,899,232</u>	<u>\$ 7,992</u>	<u>3,672,885</u>	<u>\$ —</u>	<u>\$ 1,788</u>	<u>\$ 27</u>	<u>\$ (10,532)</u>	<u>\$ (8,717)</u>

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AVALANCHE BIOTECHNOLOGIES, INC.
(a development stage company)
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	YEARS ENDED DECEMBER 31,		PERIOD FROM JULY 17, 2006 (DATE OF INCEPTION) TO DECEMBER 31,	FOR THE THREE MONTHS ENDED MARCH 31,		PERIOD FROM JULY 17, 2006 (DATE OF INCEPTION) TO MARCH 31,
	2012	2013	2013	2013	2014	2014
				(unaudited)	(unaudited)	(unaudited)
CASH FLOWS FROM OPERATING ACTIVITIES:						
Net loss	\$(1,811)	\$(5,276)	\$ (8,869)	\$ (49)	\$ (1,663)	\$ (10,532)
Adjustments to reconcile net loss to net cash used in operating activities:						
Depreciation	1	26	28	4	9	37
Stock-based compensation	76	515	616	68	115	731
Non-cash research and development expense	8	—	21	—	—	21
Non-cash interest expense	5	53	79	8	14	93
Amortization of debt issuance costs	3	20	24	5	—	24
Change in fair value of embedded derivative liability	(6)	(18)	(24)	(3)	—	(24)
Change in fair value of warrants liabilities	(13)	92	74	1	37	111
Loss on extinguishment of related-party convertible notes	—	1,671	1,671	—	—	1,671
Non-cash collaboration acquisition costs associated with sale of Series A convertible preferred stock	—	812	812	—	—	812
Changes in operating assets and liabilities:						
Accounts receivable	—	(7)	(8)	(5)	(225)	(233)
Prepaid expenses and other assets	(18)	(293)	(316)	(376)	(150)	(466)
Deposit	—	(144)	(144)	—	—	(144)
Accounts payable	445	286	806	374	178	984
Accrued expenses and other liabilities	43	80	398	(171)	269	667
Deferred rent	—	8	8	—	69	77
Net cash used in operating activities	(1,267)	(2,175)	(4,824)	(144)	(1,347)	(6,171)
CASH FLOWS FROM INVESTING ACTIVITIES:						
Purchase of property and equipment	(3)	(91)	(97)	(78)	(47)	(144)
Net cash used in investing activities	(3)	(91)	(97)	(78)	(47)	(144)
CASH FLOWS FROM FINANCING ACTIVITIES:						
Proceeds from issuance of convertible preferred stock	—	1,000	3,377	—	—	3,377
Issuance costs related to convertible preferred stock	—	(20)	(91)	—	—	(91)
Proceeds from issuance of convertible notes	—	—	100	—	—	100
Proceeds from issuance of related-party convertible notes	500	1,500	2,097	300	1,000	3,097
Net cash provided by financing activities	500	2,480	5,483	300	1,000	6,483
Effect of foreign exchange rate on cash	9	(7)	2	1	(1)	1
NET INCREASE (DECREASE) IN CASH	(761)	207	564	79	(395)	169
CASH—Beginning of period	1,118	357	—	357	564	—
CASH—End of period	\$ 357	\$ 564	\$ 564	\$ 436	\$ 169	\$ 169
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION—Cash paid for interest	\$ —	\$ —	\$ —	\$ —	\$ 5	\$ 5
SUPPLEMENTAL DISCLOSURES OF NONCASH INVESTING AND FINANCING INFORMATION						
Deferred stock issuance costs	\$ —	\$ 50	\$ 50	\$ —	\$ 46	\$ 96
Warrants issued in connection with license agreements	\$ 3	\$ —	\$ 16	\$ —	\$ 41	\$ 57
Conversion of related-party convertible notes and accrued interest to convertible preferred stock	\$ —	\$ 2,059	\$ 2,277	\$ —	\$ —	\$ 2,277

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Table of Contents**AVALANCHE BIOTECHNOLOGIES, INC.
(a development stage company)****Notes to Consolidated Financial Statements****1. Description of the business**

Nature of Business—Avalanche Biotechnologies, Inc. (the “Company”, “we” or “us”) was incorporated in Delaware on July 17, 2006, and is headquartered in Menlo Park, California. The Company was formed to develop, manufacture and market products for sustained delivery of therapeutic proteins to the eye to treat ophthalmologic disorders. On February 15, 2012, the Company established Avalanche Australia Pty Ltd, a wholly owned foreign subsidiary in Australia. Since the Company's inception, it has devoted its efforts principally to performing research and development activities, including early clinical trials, filing patent applications, obtaining regulatory approvals, hiring personnel, and raising capital to support these activities. As a result, the Company is considered a development stage company.

2. Summary of significant accounting policies and basis of presentation

Basis of Presentation—The accompanying consolidated financial statements have been prepared on a going-concern basis, which contemplates the realization of assets and the satisfaction of liabilities in the normal course of business. The Company has incurred net losses since inception and has a working capital deficit of \$0.9 million, and an accumulated deficit of \$10.5 million as of March 31, 2014. The Company has financed its operations primarily with the proceeds from the sale of preferred stock and the issuance of convertible notes. The Company's long-term success is dependent upon its ability to successfully develop, commercialize and market its products, earn revenue, obtain additional capital when needed, and, ultimately, to achieve profitable operations.

The Company's management expects that cash and cash equivalents as of March 31, 2014, when combined with the \$52.9 million gross proceeds from the Series B financing received in April 2014 and the \$8.0 million received in connection with the research collaboration and license agreement entered into with Regeneron in May 2014 (refer to Note 16), will be sufficient to fund the Company's operations through at least December 31, 2015.

Principles of Consolidation—The consolidated financial statements have been prepared in accordance with GAAP and include the accounts of the Company and its wholly-owned subsidiary. All intercompany transactions and balances have been eliminated in consolidation.

Unaudited Pro Forma Balance Sheet Information—The unaudited pro forma consolidated balance sheet information as of March 31, 2014, assumes the following capital stock transactions: (i) sale of 7,025,888 shares of Series B convertible preferred stock for approximately \$52.9 million in cash in April 2014; (ii) borrowing of \$1.0 million through convertible notes issued in April 2014 that together with \$1.0 million of outstanding notes as of March 31, 2014 were converted to 295,115 shares of Series B convertible preferred stock and resulted in the reversal of a \$2.0 million beneficial conversion feature recorded as a decrease in additional paid in capital and a \$222,000 loss on convertible notes extinguishment; (iii) repurchase of 531,208 shares of Series A convertible preferred stock for \$4.0 million in cash in April 2014; (iv) cash exercise of all outstanding warrants and subsequent conversion of shares into common stock that will occur upon the closing of this initial public offering (IPO); (v) conversion of Series A (3,368,024 shares) and Series B (7,321,003 shares) convertible preferred stock into 10,689,027 shares of common stock upon closing of IPO.

Foreign Currency Translation—The Company's consolidated financial statements are prepared in U.S. dollars. Its foreign subsidiary uses the Australian dollar as its functional currency and maintains its records in the local currency. Assets and liabilities are re-measured at exchange rates in effect at the end of the reporting period. Equity is measured at historical rates and income and expenses are re-measured at average exchange rates for the reporting period. The resulting foreign currency translation adjustment is recorded in other comprehensive income (loss) in the consolidated balance sheets and in the consolidated statements of operations and comprehensive loss. Transactions denominated in foreign currency are translated at exchange rates at the date of transaction with foreign currency gains (losses) recorded in other income (expense), net in the consolidated statements of operations and other comprehensive loss.

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Use of Estimates—The preparation of financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets, liabilities, and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of income and expenses during the reporting period. The Company bases estimates and assumptions on historical experience when available and on various factors that it believes to be reasonable under the circumstances. On an ongoing basis, the Company evaluates its estimates and assumptions, including those related to clinical trial accruals, fair value of embedded derivative liability, fair value of convertible preferred stock, and fair values of common and convertible preferred stock warrants, stock-based compensation and income taxes. The Company's actual results may differ from these estimates under different assumptions or conditions. There have been no significant changes from our original estimates in any periods presented.

Cash and Cash Equivalents—The Company considers all highly liquid investments purchased with original maturities of 90 days or less at acquisition to be cash equivalents. At December 31, 2012 and 2013, and March 31, 2014 the Company's cash was comprised of funds held in non-interest bearing bank checking accounts.

Deposit—Deposit in the amount of \$144,000 represents amounts paid in connection with the Company's facility lease agreement recorded as a long-term asset.

Segment Reporting—The Company operates and manages its business as one reporting and operating segment, which is the business of developing and commercializing therapeutics. The Company's chief executive officer, who is the chief operating decision maker, reviews financial information on an aggregate basis for purposes of allocating resources and evaluating financial performance.

Concentrations of Credit Risk and Other Uncertainties—Cash is a financial instrument that potentially subject the Company to concentrations of credit risk. Substantially all of the Company's cash was deposited in accounts at two financial institutions, and amounts may exceed federally insured limits. Management believes that the Company is not exposed to significant credit risk due to the financial strength of the depository institutions in which the cash is held.

The Company is subject to certain risks and uncertainties, including, but not limited to changes in any of the following areas that the Company believes could have a material adverse effect on future financial position or results of operations: ability to obtain future financing; regulatory approval and market acceptance of, and reimbursement for, the Company's product candidates; performance of third-party clinical research organizations and manufacturers; development of sales channels; protection of the intellectual property; litigation or claims against the Company based on intellectual property, patent, product, regulatory or other factors; and the Company's ability to attract and retain employees necessary to support the growth.

Property and Equipment—Property and equipment are recorded at cost, net of accumulated depreciation. Depreciation is recorded using the straight-line method over the estimated useful lives of the assets, generally three to five years. Leasehold improvements are capitalized and amortized over the shorter period, expected life or lease term. Major replacements and improvements are capitalized, while general repairs and maintenance are expensed as incurred.

Long-Lived Assets—We evaluate the carrying amount of our long-lived assets whenever events or changes in circumstances indicate that the assets may not be recoverable. An impairment loss would be recognized when estimated future cash flows expected to result from the use of the asset and its eventual disposition is less than the carrying amount of the asset. To date, there have been no such impairment losses.

Convertible Preferred Stock—The Company recorded issued convertible preferred stock at fair value on the dates of issuance, net of issuance costs. The convertible preferred stock is recorded outside of stockholders' deficit because the shares contain liquidation features that are not solely within the Company's control. The Company has elected not to adjust the carrying values of the convertible preferred stock to the liquidation preferences of such shares because it is uncertain whether or when an event would occur that would obligate the Company to pay the liquidation preferences to holders of shares of convertible preferred stock. Subsequent adjustments to the carrying values to the liquidation preferences will be made only when it becomes probable that such a liquidation event will occur.

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Derivative Instruments—The Company has recorded as an embedded derivative liability the potential payments that would be made to holders of the convertible notes in the event of a change of control prior to the maturity date of the convertible notes. The embedded derivative liability is initially recorded at fair value, with gains and losses arising from changes in fair value recognized in the consolidated statements of operations and comprehensive loss at each period end while such instruments are outstanding. The liability is being valued using a probability-weighted expected return model (refer to Note 3). In November 2013, the liability terminated upon the conversion of the notes into Series A convertible preferred stock (refer to Note 8).

The Company has also recorded convertible preferred stock warrants issued to investors and note holders as derivative liabilities. The convertible preferred stock warrants are initially recorded at fair value, with gains and losses arising from changes in fair value recognized in other income (expense) in the consolidated statements of operations and comprehensive loss at each period end while such instruments are outstanding and classified as long-term liabilities. The fair value of the convertible preferred stock warrants issued to convertible note holders in 2010 was recorded as non-cash interest expense in the consolidated statements of operations and comprehensive loss.

The Company has also recorded as a derivative liability the Company's obligation to issue common stock warrants in connection with license agreements as the terms of the warrants are not fixed due to potential adjustments in the exercise price. The derivative liability associated with the common stock warrants is initially recorded at fair value, with gains and losses arising from changes in fair value recognized in other income (expense), net in the consolidated statements of operations and comprehensive loss at each period end while such instruments are classified as liabilities. In March 2014, the liability terminated upon the issuance of common stock warrants and was recorded to additional paid-in capital.

Both the preferred stock and common stock warrant liabilities were valued using a Black-Scholes valuation model (refer to Note 10).

Revenue Recognition—To date, we have not generated any revenue from the sale of our products. As of December 31, 2013, we had only generated revenue from government grants. In fiscal 2014, we began to recognize license revenue from an agreement related to the licensing of certain of our intellectual property.

Government grants provide funds for certain types of expenditures in connection with research and development activities over a contractually defined period. Revenue related to government grants is recognized in the period during which the related costs are incurred and the related services are rendered, provided that the applicable performance obligations under the government grants have been met. We intend to continue to evaluate pursuing additional government grant opportunities on a case-by-case basis.

Funds received under government grants are recorded as revenue if we are deemed to be the principal participant in the contract arrangements because the activities under the contracts are part of our development programs. If we are not the principal participant, the funds from government grants are recorded as a reduction to research and development expense. Funds received from government grants are not refundable and are recognized when the related qualified research and development expenses are incurred and when there is reasonable assurance that the funds will be received. Funds received in advance of the performance of the services are recorded as deferred revenue.

Research and Development Expenses—Research and development expenses are charged to expense as incurred. Research and development expenses include certain payroll and personnel expenses, laboratory supplies, consulting costs, external contract research and development expenses, and allocated overhead, including rent, equipment depreciation and utilities. Advance payments for goods or services for future research and development activities are deferred and expensed as the goods are delivered or the related services are performed.

The Company estimates preclinical studies and clinical trial expenses based on the services performed pursuant to contracts with research institutions and clinical research organizations that conduct and manage preclinical studies and clinical trials on the Company's behalf. In accruing service fees, the Company estimates the time period over which services will be performed and the level of effort to be expended in each period. These estimates are based on communications with the third party service providers and our estimates of accrued expenses and on information available at each balance sheet date. If the actual timing of the performance of services or the level of effort varies

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from the estimate, the Company will adjust the accrual accordingly. There have been no significant changes from our original estimates in any of the periods presented.

The Company received tax credits from the Australian government in connection with certain research costs incurred in conducting research by the Company's Australian subsidiary. These refunds do not depend on the taxable income or tax position of the Company and therefore the Company does not account for them under an income tax accounting model. The Company recognizes such refunds as government grants in the period when qualified expenses are incurred as a reduction of research expenses. The Company has recorded the reimbursement of \$750,000, \$518,000 and \$46,000 from the Australian tax authorities as a reduction of research and development expense in the consolidated statements of operations and comprehensive loss in the year ended December 31, 2013 and for the three months ended March 31, 2013 and 2014, respectively.

Fair Value Measurements—Fair value is defined as the price that would be received to sell an asset or paid to transfer a liability in an orderly transaction between market participants at the measurement date. As such, fair value is a market-based measurement that should be determined based on assumptions that market participants would use in pricing an asset or liability. The carrying amounts of the Company's financial instruments, including cash, prepaid and other current assets, accounts payable and accrued expenses and other liabilities, and related-party convertible notes approximate fair value due to their short-term maturities. Refer to Note 3 for the methodologies and assumptions used in valuing financial instruments.

Stock-Based Compensation Expense—Stock-based compensation expense related to awards to employees is measured at the grant date based on the fair value of the award. The fair value of the award that is ultimately expected to vest is recognized as expense on a straight-line basis over the requisite service period, which is generally the vesting period. The expense recognized for the portion of the award that is expected to vest has been reduced by an estimated forfeiture rate. The forfeiture rate is determined at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates.

The Company uses the Black-Scholes valuation model as the method for determining the estimated fair value of certain financial instruments.

Expected Term—The expected term assumption represents the period that the Company's stock-based awards are expected to be outstanding and is determined using the simplified method.

Expected Volatility—Expected volatility is estimated using comparable public companies volatility for similar terms.

Expected Dividend—The Black-Scholes valuation model calls for a single expected dividend yield as an input. The Company has never paid dividends and has no plans to pay dividends.

Risk-Free Interest Rate—The risk-free interest rate is based on the U.S. Treasury zero-coupon issues in effect at the time of grant for periods corresponding with the expected term of option.

Stock-based compensation expense related to awards to non-employees is recognized based on the then-current fair value at each measurement date over the associated service period of the award, which is generally the vesting term, using the accelerated attribution method. The fair value of non-employee stock options is estimated using the Black-Scholes valuation model with assumptions generally consistent with those used for employee stock options, with the exception of the expected term, which is the remaining contractual life at each measurement date. Refer to Note 12 for more information on assumptions used in estimated stock-based compensation expense.

Income Taxes—The Company accounts for income taxes using the asset and liability method. The Company recognizes deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse.

In evaluating the ability to recover its deferred income tax assets, the Company considers all available positive and negative evidence, including its operating results, ongoing tax planning and forecasts of future taxable income on a

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jurisdiction-by-jurisdiction basis. In the event the Company determines that it would be able to realize its deferred income tax assets in the future in excess of their net recorded amount, it would make an adjustment to the valuation allowance that would reduce the provision for income taxes. Conversely, in the event that all or part of the net deferred tax assets are determined not to be realizable in the future, an adjustment to the valuation allowance would be charged to earnings in the period when such determination is made. As of December 31, 2012 and 2013, the Company has recorded a full valuation allowance on its deferred tax assets.

Tax benefits related to uncertain tax positions are recognized when it is more likely than not that a tax position will be sustained during an audit. Interest and penalties related to unrecognized tax benefits are included within the provision for income tax.

Comprehensive Loss—Comprehensive loss is comprised of net loss and other comprehensive income or loss. Other comprehensive income or loss consists of foreign currency translation adjustments related to translation of the financial statements of the Australian subsidiary.

Basic and Diluted Net Loss Per Share—Basic net loss per common share is computed by dividing the net loss attributable to common stockholders by the weighted-average number of common shares outstanding during the period. Diluted net loss per common share is computed by dividing the net loss by the weighted-average number of common shares and dilutive common share equivalents outstanding during the period. Because the Company has reported a net loss for all periods presented, diluted net loss per common share is the same as basic net loss per common share for those periods. Our convertible preferred stock are considered to be participating securities as they are entitled to participate in undistributed earnings with shares of common stock. Due to net losses, there is no impact on earnings per share calculation in applying the two-class method since the participating securities have no legal requirement to share in any losses (refer to Note 15).

Unaudited Pro Forma Net Loss per Share—The unaudited pro forma basic and diluted net loss per share for the year ended December 31, 2013 and the three months ended March 31, 2014 has been computed using the weighted average number of shares of common stock outstanding after giving pro forma effect to (i) the conversion of all outstanding shares of Series A convertible preferred stock as if the conversion had occurred at the earlier of the beginning of the period or the date of issuance, (ii) the issuance of Series B convertible preferred stock issued in April 2014 as if it had been outstanding as of January 1, 2014 and had automatically converted into common stock on that date, (iii) the conversion of related party convertible notes to common stock upon the date of issuance of each tranche and (iv) the exercise of all outstanding warrants to common stock as if the exercise had occurred at the earlier of the beginning of the period or the date of issuance. Net loss was adjusted to remove stock warrant changes in fair value that were recorded in other income (expense), as these warrants will be exercised upon the closing of the IPO and would not be remeasured. Net loss was also adjusted to remove interest expense on convertible notes, which was recorded in interest expense, as these notes would convert to common stock upon the closing of the IPO. The pro forma net loss per share attributable to common stockholders does not include the shares expected to be sold and related proceeds to be received from the IPO. Refer to Note 15 for further details and the calculation.

Recently Issued Accounting Pronouncements—In July 2013, the Financial Accounting Standards Board issued a new accounting standard to clarify that an unrecognized tax benefit, or a portion thereof, should be presented in the financial statements as a reduction to a deferred tax assets for a net operating loss (NOL) carryforward, a similar tax loss, or a tax credit carryforward, except to the extent not available at the reporting date to settle any additional income taxes that would result from disallowance of a tax position, or the tax law does not require the entity to use and the entity does not intend to use the deferred tax asset for such a purpose, in which case the unrecognized tax benefit should be presented as a liability. We were required to adopt this new standard effective January 1, 2014. The adoption did not have a significant impact on our disclosure, financial position, and results of operations.

3. Fair Value Measurements and Fair Value of Financial Instruments

The authoritative guidance on fair value measurements establishes a three-tier fair value hierarchy for disclosure of fair value measurements as follows:

Level 1: Quoted prices in active markets for identical assets or liabilities.

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Level 2: Observable inputs other than Level 1 prices, such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities.

Level 3: Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability.

The Company's financial instruments have consisted of Level 3 liabilities. In certain cases where there is limited activity or less transparency around inputs to valuation, securities are classified as Level 3 within the valuation hierarchy. Level 3 liabilities that are measured at estimated fair value on a recurring basis consist of common and preferred stock warrant liabilities and change in control provision embedded derivative liability.

The estimated fair values of the outstanding common and preferred stock warrant liabilities are measured using the Black-Scholes valuation model. This method of valuation involves using such inputs as the estimated fair value of the underlying stock at the measurement date, the expected term, which is the remaining contractual term of the warrants, risk-free interest rates, expected dividends on stock and expected volatility of the price of the underlying stock (refer to Note 10). Due to the nature of these inputs, the valuation of the warrants is considered a Level 3 measurement. The convertible preferred stock and common stock warrant liabilities will increase or decrease each period based on the fluctuations of the fair value of the underlying security. A significant fluctuation in the common or convertible preferred stock fair value would result in a material change in the fair values of the convertible preferred stock and common stock warrant liabilities.

The estimated fair value of the change in control embedded derivative liability was determined using a probability-weighted expected return model. The probability of a change in control occurring was determined to be 5% during fiscal 2012 and 2013. The future cash flows were discounted to their net present value using a discount rate of 21% at each measurement date. The embedded derivative liability increases or decreases each period based on the remaining unused line of credit available at each measurement date. This liability ceased in November 2013 upon the conversion of the convertible notes into Series A convertible preferred stock (refer to Note 8).

During the periods presented, the Company has not changed the manner in which it values liabilities that are measured at estimated fair value using Level 3 inputs. There were no transfers within the hierarchy during the years ended December 31, 2012 and 2013 and the three months ended March 31, 2014.

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As of December 31, 2012 and 2013 and March 31, 2014, financial assets measured and recognized at fair value on a recurring basis and classified under the appropriate level of the fair value hierarchy as described above were as follows (in thousands):

	TOTAL CARRYING VALUE	QUOTED PRICES IN ACTIVE MARKETS (LEVEL 1)	SIGNIFICANT OTHER OBSERVABLE INPUTS (LEVEL 2)	SIGNIFICANT UNOBSERVABLE INPUTS (LEVEL 3)
December 31, 2012				
Liabilities:				
Preferred stock warrant liability	\$ 36	\$ —	\$ —	\$ 36
Common stock warrant liability	5	—	—	5
Embedded derivative liability	18	—	—	18
Total liabilities	<u>\$ 59</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 59</u>
December 31, 2013				
Liabilities:				
Preferred stock warrant liability	\$ 91	\$ —	\$ —	\$ 91
Common stock warrant liability	42	—	—	42
Total liabilities	<u>\$ 133</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 133</u>
March 31, 2014 (unaudited)				
Liability:				
Preferred stock warrant liability	<u>\$ 129</u>	<u>\$ —</u>	<u>\$ —</u>	<u>\$ 129</u>

The following table provides a summary of changes in the estimated fair value of the Company's warrants liabilities and embedded derivative liability measured at estimated fair value using significant Level 3 inputs (in thousands):

	CONVERTIBLE PREFERRED STOCK WARRANT LIABILITY	COMMON STOCK WARRANT LIABILITY	EMBEDDED DERIVATIVE LIABILITY
Balance—January 1, 2012	\$ 49	\$ —	\$ —
Obligation to issue a warrant	—	5	—
Embedded derivative on notes payable issuance	—	—	24
Change in fair value	(13)	—	(6)
Balance—December 31, 2012	36	5	18
De-recognition of embedded derivative upon convertible notes conversion	—	—	(18)
Change in fair value	55	37	—
Balance—December 31, 2013	91	42	—
Issuance of common stock warrant (unaudited)	—	(41)	—
Change in fair value (unaudited)	38	(1)	—
Balance—March 31, 2014 (unaudited)	<u>\$ 129</u>	<u>\$ —</u>	<u>\$ —</u>

The changes in the estimated fair value of the warrant liabilities are recorded as other income (expense), net in the consolidated statements of operations and comprehensive loss.

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University of California—In May 2010, the Company entered into a license agreement, as amended, with the Regents for exclusive rights in the United States to certain patents owned by the Regents. Under the terms of the agreement, the Company paid an up-front license fee of \$100,000 and agreed to reimburse the Regents for patent-related expenses. The Company is obligated to pay the Regents royalties on net sales, if any, as well as an annual maintenance fee of \$50,000 beginning in the calendar year after the first commercial sale of a licensed product and milestone payments related to the achievement of certain clinical and regulatory goals totaling up to \$900,000 for the first indication and \$500,00 for each additional indication for up to two additional indications. Through December 31, 2013, none of these goals had been achieved, and no milestones were payable.

5. Property and Equipment, Net

Property and equipment, net, as of December 31, 2012 and 2013 and March 31, 2014 consists of the following (in thousands):

	<u>DECEMBER 31,</u>		<u>MARCH 31,</u>
	<u>2012</u>	<u>2013</u>	<u>2014</u>
			(unaudited)
Office and computer equipment	\$ 6	\$ 10	\$ 28
Laboratory equipment	—	87	97
Leasehold improvements	—	—	19
Total property and equipment	6	97	144
Less accumulated depreciation	(2)	(28)	(37)
Property and equipment, net	<u>\$ 4</u>	<u>\$ 69</u>	<u>\$ 107</u>

Depreciation expense related to property and equipment was \$1,000, \$26,000 and \$28,000 for the years ending December 31, 2012, and 2013, and for the period from July 17, 2006 (date of inception) to December 31, 2013, respectively. Depreciation expense for the three month period ended March 31, 2013 and 2014 was \$4,000 and \$9,000, respectively. Depreciation expense for the period from July 17, 2006 (date of inception) through March 31, 2014 was \$37,000.

6. Accrued Expenses and Other Current Liabilities

Accrued expenses and other current liabilities as of December 31, 2012 and 2013 and March 31, 2014 consist of the following (in thousands):

	<u>DECEMBER 31,</u>		<u>MARCH 31,</u>
	<u>2012</u>	<u>2013</u>	<u>2014</u>
			(unaudited)
Accrued license fee payable	\$ 181	\$ —	\$ 6
Employee compensation	117	162	260
Accrued professional fees	13	162	249
Accrued clinical costs	—	54	144
Other	6	15	3
	<u>\$ 317</u>	<u>\$ 393</u>	<u>\$ 662</u>

7. Commitments and Contingencies**Facility Lease Agreement**

On December 20, 2013, the Company entered into a six-year building lease in Menlo Park, California. The Company may extend this lease for up to four years. The lease agreement provides for an escalation of rent payments each year. The Company records rent expense on a straight-line basis over the term of the lease.

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As of December 31, 2013, future minimum commitments under facility operating leases were as follows (in thousands):

<u>YEARS ENDED DECEMBER 31,</u>	<u>TOTAL LEASE COMMITMENTS</u>
2014	\$ 120
2015	269
2016	302
2017	311
2018	320
2019 and thereafter	441
Total minimum lease payments	<u>\$ 1,763</u>

Rent expense recognized under all operating leases, including additional rent charges for utilities, parking, maintenance, and real estate taxes was \$17,000 and \$53,000 for the years ended December 31, 2012 and 2013, respectively. Rent expense for the period from July 17, 2006 (date of inception) through December 31, 2013 was \$76,000. Rent expense was \$8,000, \$117,000, and \$193,000 for the three month periods ended March 31, 2013 and 2014 and for the period from July 17, 2006 (date of inception) through March 31, 2014, respectively.

Collaborations and License Agreements

The Company is party to various agreements, principally relating to licensed technology that requires future payments relating to milestones or royalties on future sales of specified products. Through December 31, 2013, none of the goals had been achieved under the license agreements and no cash milestones were accrued or payable. Because the achievement of these milestones is not fixed and determinable, such commitments have not been included on the Company's consolidated balance sheets. Aggregate annual maintenance fees payable in 2014 are approximately \$46,000 under these agreements.

Guarantees and Indemnifications

In the normal course of business, the Company enters into agreements that contain a variety of representations and provide for general indemnification. The Company's exposure under these agreements is unknown because it involves claims that may be made against the Company in the future. To date, the Company has not paid any claims or been required to defend any action related to its indemnification obligations. As of December 31, 2013, the Company does not have any material indemnification claims that were probable or reasonably possible and consequently has not recorded related liabilities.

8. Related-Party Convertible Notes***2006-2009 Convertible Notes***

Between December 2006 and September 2009, the Company issued a series of convertible notes agreements (2006-2009 Notes) with investors to borrow up an aggregate of \$197,000. In connection with the 2006-2009 Notes, the Company agreed to issue warrants for common and convertible preferred stock. In September 2010, the principal and accrued interest of \$217,000 converted into an aggregate of 149,979 shares of Series A convertible preferred stock at \$1.45 per share. In September 2010, the Company issued warrants to purchase 59,000 shares of common stock and warrants to purchase 54,716 shares of Series A convertible preferred stock (refer to Note 10).

2012 Related-Party Convertible Notes

On August 28, 2012, the Company entered into a convertible note payable agreement (2012 Notes) with a related party investor for the issuance of up to an aggregate principal amount of \$2.0 million of convertible notes. The 2012 Notes were due to mature on February 28, 2014 and accrue interest at a rate of 5% per year. In November 2012, the Company borrowed \$0.5 million of 2012 Notes. During February, April, July and September 2013, the Company borrowed the remaining aggregate principal amount of \$1.5 million of 2012 Notes.

Upon occurrence of a change of control transaction prior to the maturity date, 130% of \$2.0 million minus the outstanding principal balance would be payable to the investor. The change of control provision met the accounting

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definition of an embedded derivative and required bifurcation. The Company valued this embedded derivative on the 2012 Notes using a probability-weighted model which included significant estimates regarding the expected time to a change of control event, and a discount rate. The estimated fair value of this embedded derivative on the date of issuance was determined to be approximately \$24,000, and was recorded as a discount to the 2012 Notes. This discount was amortized to interest expense through the maturity date of the 2012 Notes. The embedded derivative was re-measured each period end with changes in fair value recorded in the consolidated statements of operations and comprehensive loss. In November 2013, the derivative terminated upon the conversion of the 2012 Notes into Series A convertible preferred stock.

In November 2013, the Company amended the 2012 Notes agreement to provide for the acceleration of the conversion of the 2012 Notes into shares of Series A convertible preferred stock. The outstanding principal and accrued and unpaid interest of \$2.1 million was converted into 1,419,959 shares of Series A convertible preferred stock at \$1.45 per share. The 2012 Notes modification was recorded as a \$1.7 million loss on extinguishment of related-party convertible notes in the consolidated statement of operations and comprehensive loss (refer to Note 9).

2013 Related-Party Convertible Notes

On October 22, 2013, the Company entered into a convertible note purchase agreement (2013 Notes) with a related party investor for the issuance and sale of up to an aggregate principal amount of \$5.0 million of convertible notes. In each of January 2014 and April 2014, the Company borrowed an aggregate principal amount of \$1.0 million of 2013 Notes.

The 2013 Notes mature on December 31, 2016 and accrue interest at a rate of 5% per year. The 2013 Notes and any accrued and unpaid interest are automatically convertible into equity securities sold in the next qualified round of financing occurring prior to the maturity date, at the conversion price equal to 90% of the original issuance price of such equity securities sold in such next round of financing. Upon maturity, the 2013 Notes will automatically convert into shares of Series A convertible preferred stock at a conversion price of \$1.45 per share. Upon a change in control event, all of the outstanding principal and accrued interest becomes immediately payable.

The difference between the fair value of the securities into which the debt was convertible and the effective conversion price on the borrowing date represents a beneficial conversion feature. In connection with the January 2014 and April 2014 borrowings, the Company recorded the fair value of the beneficial conversion feature of \$1.0 million and \$1.0 million, respectively, by allocating a portion of the proceeds to additional paid-in capital, resulting in a discount on the convertible instrument, which is being amortized over the repayment period using the effective interest method. Because of the recording of \$1.0 million beneficial conversion feature, the carrying value of the 2013 Notes as of March 31, 2014 was equal to the accrued interest balance of \$14,000, net of the associated discount.

In April 2014, the Company sold a qualified round of financing (refer to Note 16), and the outstanding balance of the 2013 Notes converted into 295,115 shares of Series B convertible preferred shares at a conversion price \$6.78 equal to 90% of the original issuance price of \$7.53 per share.

9. Convertible Preferred Stock

From inception to December 31, 2011 the Company issued 1,789,618 shares Series A convertible preferred stock to investors for cash or upon conversion of convertible notes and accrued interest at \$1.45 per share.

In November 2013, the Company issued 1,419,959 shares of Series A convertible preferred stock upon the conversion of the 2012 Notes (refer to Note 8) and issued 689,655 shares to a potential collaborator for cash at \$1.45 per share. The estimated fair value of Series A convertible preferred stock was \$2.63 per share on the issuance date. The fair value of the Series A convertible preferred stock was determined using a PWERM model, a scenario-based analysis that estimates the value per share based on the probability-weighted present value of expected future investment returns, considering several possible outcomes for the Company in the future, as well as the economic and control rights of each share class. In the November 2013 valuation, the Company considered the estimated fair value of the Series A preferred stock under three potential scenarios, including an initial public offering, a collaborative partnering agreement model, and a corporate failure.

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The Company recorded the difference between the effective conversion price and the fair value of the securities into which the debt was converted; resulting in a loss on extinguishment for the 2012 Notes (refer to Note 8). The Company also recorded expense of \$0.8 million associated with the intrinsic value of the convertible preferred Series A shares issued to a potential collaborator, which is recorded in general and administrative expense in the consolidated statements of operations and comprehensive loss for the year ended December 31, 2013.

The authorized, issued and outstanding shares of Series A convertible preferred stock and liquidation preferences as of December 31, 2012 and 2013 and March 31, 2014 were as follows (in thousands, except share numbers):

SERIES	SHARES		LIQUIDATION AMOUNT	CARRYING VALUE
	AUTHORIZED	OUTSTANDING		
As of December 31, 2012	2,123,681	1,789,618	\$ 2,595	\$ 2,471
As of December 31, 2013	4,233,295	3,899,232	\$ 5,654	\$ 7,992
As of March 31, 2014 (unaudited)	4,233,295	3,899,232	\$ 5,654	\$ 7,992

The Series A convertible preferred stock rights, privileges and preferences are as follows:

Conversion Rights—Each share of Series A convertible preferred stock is convertible at an option of the holder into one share of common stock (subject to adjustment for certain events, including dilutive issuances, stock splits, and reclassifications). The Series A convertible preferred stock will also be converted automatically into shares of common stock (1) immediately prior to an initial public offering with aggregate proceeds of at least \$50 million or (2) upon the date specified by written consent of holders of a majority of the outstanding preferred shares on an as-converted basis.

Dividends—Each holder is entitled to 8% noncumulative dividends per share, if and when declared by the board of directors. The 8% noncumulative dividends are to be paid in advance of any distributions to common stock holders. Each holder is also entitled to participate in dividends on an as-converted pari passu basis together with common stock after distribution of 8% noncumulative dividends. No dividends have been declared to date.

Voting—Each holder has the right to one vote for each share of common stock into which such Series A convertible preferred stock could be converted. Certain financing, acquisition, disposition, and recapitalization transactions require the vote of the majority of the shares of outstanding Series A convertible preferred stock, provided that at least 1,000,000 shares of convertible preferred stock are issued and outstanding.

Liquidation Preference—In the event of any liquidation, dissolution, or winding-up of the Company, including a merger, acquisition, or sale of assets, as defined, each Series A convertible preferred stock holder is entitled to receive the greater of i) an amount of \$1.45 per share for each share of Series A convertible preferred stock held (as adjusted for recapitalizations, stock combinations, stock dividends, stock splits, and reclassifications), plus any declared but unpaid dividends prior to and in preference to any distribution to the holders of common stock or ii) an amount of cash, securities or other property per share on as-converted to common stock basis. If the assets of the Company are insufficient to make payment in full to all Series A convertible preferred stock holders than the assets or consideration will be distributed ratably among such holders.

Any remaining assets would then be distributed among the holders of the common stock on a pro rata basis based on the number of shares of common stock held by them.

Election of Board of Directors—The holders of Series A convertible preferred stock, voting as a separate class, are entitled to elect one member of the board of directors. The holders of common stock, voting as a separate class, are entitled to elect two members. Convertible preferred and common stock holders, voting together as a single class, are entitled to elect any additional members of the board of directors.

10. Warrants

In March 2010, as amended in November 2011 and August 2012, the Company entered into a research collaboration agreement with the LEI. Under the terms of the agreement, LEI licensed certain intellectual property

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rights to the Company and agreed to conduct certain clinical research studies. Additionally under the agreement, the Company paid an up-front technology transfer fee and agreed to grant LEI warrants to purchase up to 400,000 shares of common stock for the achievement of certain milestones, and committed to funding the research studies to be conducted by LEI.

In August 2010, in connection with the LEI license agreement, the Company issued a warrant to purchase 125,000 shares of common stock with an exercise price of \$0.001 per share. The Company estimated the fair value of these warrants to be approximately \$10,000, which was recorded as research and development expense upon issuance. The fair value of the warrants was calculated using the Black-Scholes valuation model, and was based on the common stock fair value of \$0.08 per share, the contractual term of the warrants of 5 years, a risk-free interest rate of 1.5%, an expected volatility of 87% and a 0% expected dividend yield.

In September 2010, in connection with the sale of Series A convertible preferred stock and the conversion the 2006-2009 Notes, the Company issued warrants to purchase 54,716 shares of Series A convertible preferred stock at an exercise price of \$1.45 per share. These Series A convertible preferred stock warrants are exercisable immediately and expire on September 7, 2015. The Company estimated the fair value of these warrants as of the issuance date to be \$54,000, which was recorded as a debt discount and amortized as interest expense at the time of issuance. The fair value of the warrants was calculated using the Black-Scholes valuation model, and was based on the Series A convertible preferred stock fair value of \$1.45 per share, contractual term of the warrants of 5 years, a risk-free interest rate of 1.4%, an expected volatility of 87% and a 0% expected dividend yield. The warrants to purchase convertible preferred stock are classified as liabilities and are re-measured each reporting period. As of December 31, 2013, these warrants remained outstanding and exercisable. The fair value of these warrants was \$36,000 and \$91,000 as of December 31, 2012, and 2013, respectively and \$129,000 as of March 31, 2014.

In September 2010, in connection with the sale of Series A convertible preferred stock and the conversion the 2006-2009 Notes, the Company issued to existing investors warrants to purchase 59,000 shares of common stock with an exercise price of \$0.15 per share. These common stock warrants were exercisable immediately and expire on September 7, 2015. The Company estimated the fair value of these equity classified warrants to be approximately \$3,000 which was recorded as interest expense upon issuance and additional paid-in capital. The fair value of the warrants was calculated at the issuance date using the Black-Scholes valuation model, and was based on the common stock fair value of \$0.08 per share, contractual term of the warrants of 5 years, a risk-free interest rate of 1.4%, an expected volatility of 87% and a 0% expected dividend yield.

In connection with an amendment to the LEI license agreement, in February 2012 the Company issued to LEI a warrant to purchase 80,000 shares of common stock with an exercise price of \$0.19 per share. This common stock warrant was exercisable immediately, and expires on February 24, 2017. The Company estimated the fair value of these warrants to be approximately \$3,000 which was recorded as research and development expense and additional paid-in capital upon issuance. The fair value of the warrants was calculated using the Black-Scholes valuation model, and was based on the common stock fair value of \$0.08 per share, contractual term of the warrants of 5 years, a risk-free interest rate of 0.8%, an expected volatility of 87% and a 0% expected dividend yield.

In connection with an amendment to the LEI license agreement in August 2012 the Company agreed to issue to LEI a warrant to purchase 25,000 shares of common stock. The Company estimated the fair value of the obligation to issue these warrants to be approximately \$5,000 which was recorded as research and development expense and common stock warrant liability. The fair value of the obligation was calculated using the Black-Scholes valuation model, and was based on the common stock fair value of \$0.30 per share, contractual term of the warrants of 5 years, a risk-free interest rate of 0.7%, an expected volatility of 86% and a 0% expected dividend yield. Until the Company issued the warrant, it classified it as a common stock warrant liability and re-measured the fair value at the end of each reporting period. The fair value of this liability was \$5,000 and \$42,000 as of December 31, 2012 and 2013. In March 2014, the Company issued the common stock warrant to LEI with an exercise price of \$2.75 per share, at which time the issued common stock warrant was recorded to additional paid-in capital.

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As of December 31, 2012 and 2013, and March 31, 2014, the following warrants and obligations to issue warrants to purchase shares of common stock and convertible preferred stock were outstanding and exercisable:

WARRANT HOLDER	ISSUE DATE	ISSUED IN CONNECTION WITH	WARRANT TO PURCHASE	EXERCISABLE INTO	EXERCISE PRICE	EXPIRATION DATE
LEI	08/20/2010	License Agreement	125,000	Common	\$ 0.001	08/20/2015
LEI	02/24/2012	License Agreement	80,000	Common	\$ 0.19	02/24/2017
LEI	03/05/2014	License Agreement	25,000	Common	\$ 2.75	03/05/2019
Investors		Conversion of 2006-2009 Notes	59,000	Common	\$ 0.15	09/07/2015
Investors	09/07/2010	Conversion of 2006-2009 Notes	54,716	Series A	\$ 1.45	09/07/2015

The fair value of each warrant was estimated as of December 31, 2012 and 2013 and March 31, 2014 using the Black-Scholes valuation model with the following assumptions:

		DECEMBER 31, 2012				FAIR VALUE OF UNDERLYING SHARES
WARRANT ISSUE DATE	CLASS	EXPECTED TERM (IN YEARS)	EXPECTED VOLATILITY	RISK-FREE INTEREST RATE	DIVIDEND YIELD	
September 2010	Series A preferred stock	2.68	73%	0.4%	—	\$ 1.45
August 2012 (obligation)	Common stock	5.00	87%	0.7%	—	\$ 0.30

		DECEMBER 31, 2013				FAIR VALUE OF UNDERLYING SHARES
WARRANT ISSUE DATE	CLASS	EXPECTED TERM (IN YEARS)	EXPECTED VOLATILITY	RISK-FREE INTEREST RATE	DIVIDEND YIELD	
September 2010	Series A preferred stock	1.68	59%	0.3%	—	\$ 2.96
August 2012 (obligation)	Common stock	5.00	75%	1.6%	—	\$ 2.75

		MARCH 31, 2014 (UNAUDITED)				FAIR VALUE OF UNDERLYING SHARES
WARRANT ISSUE DATE	CLASS	EXPECTED TERM (IN YEARS)	EXPECTED VOLATILITY	RISK-FREE INTEREST RATE	DIVIDEND YIELD	
September 2010	Series A preferred stock	1.44	59%	0.1%	—	\$ 3.74

11. STOCKHOLDERS' DEFICIT

Common Stock—During the period from July 17, 2006 (date of inception) to December 31, 2013, the Company issued an aggregate of 210,000 fully vested shares and 4,550,000 restricted shares of the Company's common stock to the founders for cash consideration of \$1,000, which was the deemed fair value of the common stock at that time. The restricted shares are subject to certain restrictions regarding the transfer of such shares, including a right of first refusal by the Company in the event of any sale or other transfer of the shares. The Company has a right of repurchase with respect to early exercised restricted shares at an amount equal to the lower of (i) the exercise price of each restricted share being repurchased and (ii) the fair market value of such restricted share at the time the Company's right of repurchase is exercised. The Company's right to repurchase these shares lapses 25% after one

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year and 1/48 of the total number of shares originally granted per month for 36 months thereafter. In July and August 2010, the Company repurchased an aggregate of 1,200,000 shares of outstanding common stock from founders. As of December 31, 2013, there are no shares subject to repurchase restrictions.

Reserved Shares—The Company's reserved shares of common stock for future issuance related to potential conversion of the preferred stock, warrants exercise and exercise of stock options as of December 31, 2013 and March 31, 2014 are as follows:

	<u>DECEMBER 31, 2013</u>	<u>MARCH 31, 2014 (unaudited)</u>
Series A convertible preferred stock	3,899,232	3,899,232
Series A convertible preferred stock warrants	54,716	54,716
Options to purchase common stock	3,640,000	4,134,200
Warrants to purchase common stock	<u>264,000</u>	<u>289,000</u>
	<u>7,857,948</u>	<u>8,377,148</u>

12. STOCK OPTION PLAN

On December 26, 2006, the Company adopted 2006 Plan, which was amended by the board of directors on November 15, 2012. The 2006 Plan allows for the granting of ISOs and NSOs to the employees, members of the board of directors, and consultants of the Company. ISOs may be granted only to Company's employees, including officers and directors who are also employees. NSOs may be granted to the employees and consultants.

Options under the Plan may be granted for periods of up to 10 years and at prices no less than 100% of the estimated fair value of the shares on the date of grant as determined by the board of directors, provided, however, that the exercise price of an ISO and NSO granted to a 10% shareholder shall not be less than 110% of the estimated fair value of the shares on the date of grant. Options granted to employees and non-employees generally vest ratably over four years.

As of December 31, 2013 a total of 4,311,875 shares of common stock are authorized for issuance and 600,000 shares are available for future grant under the Plan. As of March 31, 2014 a total of 4,311,875 shares of common stock are authorized for issuance and 105,800 shares are available for future grant under the Plan.

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Activity under the Plan is set forth below:

	NUMBER OF SHARES	WEIGHTED- AVERAGE EXERCISE PRICE	WEIGHTED- AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)	AGGREGATE INTRINSIC VALUE ^(a) (IN THOUSANDS)
Balances, January 1, 2012	705,000	\$ 0.05		
Options granted	2,890,000	\$ 0.19		
Options exercised	—	—		
Options cancelled	—	—		
Balances, December 31, 2012	3,595,000	\$ 0.16	9.3	\$ 495
Options granted	45,000	\$ 0.34		
Options exercised	—	—		
Options cancelled	—	—		
Balances, December 31, 2013	3,640,000	\$ 0.16	8.3	\$ 9,411
Options granted (unaudited)	494,200	\$ 2.75		
Options exercised (unaudited)	—	—		
Options cancelled (unaudited)	—	—		
Balances, March 31, 2014 (unaudited)	<u>4,134,200</u>	\$ 0.47	8.3	\$ 11,065
Vested and expected to vest as of December 31, 2013	<u>3,579,500</u>	\$ 0.16	8.3	\$ 9,257
Exercisable as of December 31, 2013	<u>1,520,305</u>	\$ 0.13	7.6	\$ 3,988
Vested and expected to vest as of March 31, 2014 (unaudited)	<u>4,078,514</u>	\$ 0.47	8.3	\$ 10,914
Exercisable as of March 31, 2014 (unaudited)	<u>1,720,927</u>	\$ 0.14	7.5	\$ 5,182

^(a) The aggregate intrinsic value is calculated as the difference between the options exercise price and the estimated fair value of the underlying common stock.

The weighted-average fair values of options granted during fiscal years 2012 and 2013 and for three months ended March 31, 2014 were \$0.21, \$0.37 and \$1.93, respectively. There were no options granted during the three month periods ended March 31, 2013.

The following table summarizes information with respect to stock options outstanding and currently exercisable and vested.

As of December 31, 2013:

RANGE OF EXERCISE PRICES	OPTIONS OUTSTANDING		OPTIONS EXERCISABLE AND VESTED	
	NUMBER OUTSTANDING	WEIGHTED- AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)	NUMBER OUTSTANDING	WEIGHTED- AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)
\$.0001 – \$0.08	480,000	5.9	480,000	5.9
\$ 0.09 – \$0.17	225,000	6.9	170,312	6.9
\$ 0.18 – \$0.27	2,890,000	8.8	861,035	8.7
\$ 0.28 – \$0.34	45,000	9.3	8,958	9.3

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As of March 31, 2014 (unaudited):

RANGE OF EXERCISE PRICES	OPTIONS OUTSTANDING		OPTIONS EXERCISABLE AND VESTED	
	NUMBER OUTSTANDING	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)	NUMBER OUTSTANDING	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE (IN YEARS)
\$.0001 – \$0.08	480,000	5.7	480,000	5.7
\$ 0.09 – \$0.17	225,000	6.7	184,374	6.7
\$ 0.18 – \$0.27	2,890,000	8.5	1,041,659	8.5
\$ 0.28 – \$1.55	45,000	9.0	11,770	9.0
\$ 1.56 – \$2.75	494,200	9.9	3,124	9.9

The Company has recorded aggregate stock-based compensation expense related to the issuance of stock option awards to employees and nonemployees in the consolidated statement of operations and comprehensive loss as follows (in thousands):

	YEAR ENDED DECEMBER 31,		PERIOD FROM JULY 17, 2006 (DATE OF INCEPTION) TO DECEMBER 31, 2013	THREE MONTHS ENDED MARCH 31,		PERIOD FROM JULY 17, 2006 (DATE OF INCEPTION) TO MARCH 31, 2014
	2012	2013		2013 (unaudited)	2014 (unaudited)	
Research and development	\$ 54	\$ 362	\$ 441	\$ 33	\$ 69	\$ 510
General and administrative	22	153	175	35	46	221
Total	<u>\$ 76</u>	<u>\$ 515</u>	<u>\$ 616</u>	<u>\$ 68</u>	<u>\$ 115</u>	<u>\$ 731</u>

Stock Options Granted to Employees

For the years ended December 31, 2012 and 2013, and for the period from July 17, 2006 (date of inception) to December 31, 2013, the Company recorded \$20,000, \$136,000, and \$156,000, respectively, of stock-based compensation expense related to employees options. For the three months ended March 31, 2013 and 2014, and for the period from July 17, 2006 (date of inception) to March 31, 2014, the Company recorded \$33,000, \$54,000, and \$210,000, respectively, of stock-based compensation expense related to employees options. The fair value of each option issued to employees was estimated at the date of grant using the Black-Scholes valuation model with the following weighted-average assumptions:

	YEAR ENDED DECEMBER 31,		THREE MONTHS ENDED MARCH 31,	
	2012	2013	2013 (unaudited)	2014 (unaudited)
Expected volatility	82%	80%	—	78%
Expected term (in years)	6.0	6.0	—	6.0
Risk-free interest rate	0.9%	1.0%	—	1.8%
Expected dividend yield	0.0%	0.0%	—	0.0%

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As of December 31, 2013, there was \$391,000 of unrecognized stock-based compensation expense related to employees' awards that is expected to be recognized over a weighted-average period of 2.9 years. As of March 31, 2014, there was \$1.2 million of unrecognized stock-based compensation expense related to employees' awards that is expected to be recognized over a weighted-average period of 2.8 years.

Stock Options Granted to Non-Employees

Stock-based compensation expense related to stock options granted to nonemployees is recognized as the stock options are earned. The Company believes that the estimated fair value of the stock options is more readily measurable than the fair value of the services rendered. For the years ended December 31, 2012 and 2013 and for the period from July 17, 2006 (date of inception) to December 31, 2013, the Company recorded \$56,000, \$379,000, and \$460,000, respectively, of stock-based compensation expense related to non-employees options. For the three months ended March 31, 2013 and 2014, and for the period from July 17, 2006 (date of inception) to March 31, 2014, the Company recorded \$35,000, \$61,000, and \$521,000, respectively, of stock based compensation expense related to non-employees options.

We used the following weighted-average assumptions in estimating non-employees stock-based compensation expense:

	FOR THE YEAR ENDED DECEMBER 31,		FOR THE THREE MONTHS ENDED MARCH 31,	
	2012	2013	2013 (unaudited)	2014 (unaudited)
Expected volatility	78%	79%	79%	77%
Contractual term remaining (in years)	9.0	7.9	8.2	7.8
Risk-free interest rate	1.6%	1.8%	1.6%	2.6%
Expected dividend yield	0.0%	0.0%	0.0%	0.0%

Fair Value of Common Stock

In determining the exercise prices for options granted, the Company's board of directors has considered the fair value of the common stock as of each grant date the measurement date. The fair value of the common stock underlying the stock options has been determined by the board of directors at each award grant date based upon a variety of factors, including the results obtained from an independent third party valuation, the Company's financial position and historical financial performance, the status of technological developments within the Company's products, the composition and ability of the current clinical and management team, an evaluation or benchmark of the Company's competition, the current business climate in the marketplace, the illiquid nature of the common stock, arm's-length sales of the Company's capital stock (including convertible preferred stock), the effect of the rights and preferences of the preferred shareholders, and the prospects of a liquidity event, among others.

13. 401(k) Savings Plan

The Company established a defined-contribution savings plan under Section 401(k) of the Code. The 401(k) Plan covers all employees who meet defined minimum age and service requirements, and allows participants to defer a portion of their annual compensation on a pretax basis. The Company has not made any contributions to the 401(k) Plan as of December 31, 2013.

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For the years ended December 31, 2012 and 2013 and for the three months ended March 31, 2013 and 2014, the Company did not record a current or deferred income tax expense or benefit.

The following table presents domestic and foreign components of loss before provision for income taxes (in thousands):

	FOR THE YEAR ENDED DECEMBER 31,	
	2012	2013
U.S.	\$ (1,051)	\$ (5,031)
Foreign	(760)	(245)
Income (Loss) before income taxes	<u>\$ (1,811)</u>	<u>\$ (5,276)</u>

A reconciliation of income tax expense computed at the statutory federal income tax rate of 34% to income taxes as reflected in the financial statements is as follows (in thousands):

	FOR THE YEAR ENDED DECEMBER 31,	
	2012	2013
Federal income tax expense (benefit) at statutory rate	\$ (616)	\$ (1,794)
Loss on extinguishment of related-party convertible notes	—	568
Non-deductible foreign research expenses	222	26
Non-deductible expenses	5	74
Research and development tax credits	—	(93)
Change in valuation allowance	359	1,209
Foreign rate differential	30	10
Total tax expense (benefit)	<u>\$ —</u>	<u>\$ —</u>

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The following table presents significant components of the Company's deferred tax assets (in thousands):

	AS OF DECEMBER 31,	
	2012	2013
Deferred tax assets:		
Net operating loss carryforwards	\$ 827	\$ 1,876
Accruals, reserve and other	120	292
Tax credit carryforwards	13	145
Property and equipment	—	2
Intangibles	130	223
Other	1	(1)
Total deferred tax assets	<u>1,091</u>	<u>2,537</u>
Valuation allowance	(1,091)	(2,537)
Net deferred tax assets	<u>\$ —</u>	<u>\$ —</u>

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The Company has evaluated the positive and negative evidence bearing upon the realizability of its deferred tax assets. Based on the Company's history of operating losses, the Company has concluded that it is more likely than not that the benefit of its deferred tax assets will not be realized. Accordingly, the Company has provided a full valuation allowance for deferred tax assets as of December 31, 2012 and 2013. The valuation allowance increased approximately \$396,000 and \$1.4 million during the years ended December 31, 2012 and December 31, 2013, respectively, due to net operating losses.

As of December 31, 2012 and 2013 the Company had U.S. federal NOL carryforwards of approximately \$1.9 million and \$4.5 million, respectively, which may be available to offset future federal income and expire at various years beginning with 2026. As of December 31, 2012 and 2013, the Company also had U.S. state NOL carryforwards of approximately \$2.7 million and \$5.4 million, respectively, which may be available to offset future state income and expire at various years beginning with 2026. At December 31, 2012 and 2013, the Company also had approximately \$28,000 and \$70,000, respectively, of foreign net operating loss carryforwards which may be available to offset future foreign income; these carryforwards do not expire.

As of December 31, 2012 and 2013, the Company had federal research and development tax credit carryforwards of approximately \$34,000 and \$116,000, respectively, available to reduce future tax liabilities which expire at various years beginning with 2026. As of December 31, 2012 and 2013, the Company had state credit carryforwards of approximately \$25,000 and \$98,000, respectively, available to reduce future tax liabilities which do not expire.

Under Section 382 of the Internal Revenue Code of 1986, as amended (Code), our ability to utilize NOL carryforwards or other tax attributes, such as research tax credits, in any taxable year may be limited if we have experienced an "ownership change." Generally, a Section 382 ownership change occurs if there is a cumulative increase of more than 50 percentage points in the stock ownership of one or more stockholders or groups of stockholders who owns at least 5% of a corporation's stock within a specified testing period. Similar rules may apply under state tax laws. We believe that we have experienced at least two ownership changes under Section 382, which will result in limitations in our ability to utilize net operating losses and credits. In addition, we may experience ownership changes as a result of our proposed initial public offering, future offerings or other changes in the ownership of our stock. As a result, the amount of the NOLs and research and credit carryforwards presented in our financial statements could be limited and may expire unutilized.

The Company files income tax returns in the United States, and state and foreign jurisdictions. The federal, state and foreign income tax returns are open under the statute of limitations subject to tax examinations for the tax years ended December 31, 2009 through December 31, 2013. To the extent the Company has tax attribute carryforwards, the tax years in which the attribute was generated may still be adjusted upon examination by the IRS, state or foreign tax authorities to the extent utilized in a future period.

The Company has total unrecognized tax benefits as of December 31, 2012 and 2013 of approximately \$5,000 and \$43,000, respectively. No amount of the unrecognized tax benefits, if recognized, would reduce the Company's annual effective tax rate because the benefits are in the form of deferred tax assets for which a full valuation allowance has been recorded. The Company does not anticipate a significant change to its unrecognized tax benefits over the next twelve months. A reconciliation of the unrecognized tax benefits is as follows (in thousands):

	FOR THE YEAR ENDED DECEMBER 31,	
	2012	2013
Unrecognized tax benefits as of the beginning of the year	\$ —	\$ 5
Increase related to prior year tax provisions	—	7
Decrease related to prior year tax provisions	—	—
Increase related to current year tax provisions	5	31
Unrecognized tax benefits as of the end of the year	<u>\$ 5</u>	<u>\$ 43</u>

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The Company recognizes interest and penalties related to uncertain tax positions in income tax expense. As of December 31, 2012 and 2013, the Company had no accrued interest or penalties related to uncertain tax positions and no amounts have been recognized in the Company's consolidated statements of operations and comprehensive loss. There are no ongoing examinations by taxing authorities at this time.

15. Net Loss Per Share

The following table sets forth the computation of the basic and diluted net loss per share for the years ended December 31, 2012 and 2013, and for three months ended March 31, 2013 and 2014 (in thousands, except share and per share data):

	YEAR ENDED DECEMBER 31,		THREE MONTHS ENDED MARCH 31,	
	2012	2013	2013 (unaudited)	2014 (unaudited)
Net loss	\$ (1,811)	\$ (5,276)	\$ (49)	\$ (1,663)
Weighted-average common shares outstanding used to calculate basic and diluted net loss per common share:				
Shares issued	3,672,885	3,672,885	3,672,885	3,672,885
Less: restricted stock subject to repurchase	(30,382)	—	—	—
Net shares outstanding	3,642,503	3,672,885	3,672,885	3,672,885
Basic and diluted net loss per common share	\$ (0.50)	\$ (1.44)	\$ (0.01)	\$ (0.45)

The following common stock equivalents were excluded from the calculation of diluted net loss per share for the periods indicated because including them would have had an anti-dilutive effect:

	YEAR ENDED DECEMBER 31,		THREE MONTHS ENDED MARCH 31,	
	2012	2013	2013 (unaudited)	2014 (unaudited)
Options to purchase common stock	3,595,000	3,640,000	3,595,000	4,134,200
Warrants to purchase common stock	264,000	264,000	264,000	289,000
Preferred stock	1,789,618	3,899,232	1,789,618	3,899,232
Warrants to purchase preferred stock	54,716	54,716	54,716	54,716
	<u>5,703,334</u>	<u>7,857,948</u>	<u>5,703,334</u>	<u>8,377,148</u>

The unaudited pro forma basic and diluted net loss per share attributable to common stockholders for the year ended December 31, 2013 and for the three months period ended March 31, 2014 gives effect to the conversion of all shares of convertible preferred stock and the exercise of all outstanding warrants into common stock immediately prior to the closing of an initial public offering by treating all shares and warrants as if they had been converted and exercised to common stock shares in all periods in which such convertible preferred stock shares and warrants were outstanding. Capital equity transactions that occurred in April and May 2014 are included in the calculation of the weighted average shares as if they had been occurred on January 1, 2014.

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Unaudited pro forma basic and diluted net loss per share are computed as follows (in thousands, except share and per share data):

	YEAR ENDED DECEMBER 31, 2013	THREE MONTHS ENDED MARCH 31, 2014
	(unaudited)	
Pro forma loss per share—basic and diluted		
Numerator:		
Net loss—basic and diluted as reported	\$ (5,276)	\$ (1,663)
Convertible note interest	59	14
Change in fair value of preferred stock warrants	92	37
Pro forma net loss attributable to common stockholders—basic and diluted	(5,125)	(1,612)
Denominator:		
Weighted-average shares used to compute basic and diluted net loss per share	3,672,885	3,672,885
Adjustments to reflect the assumed conversion of Series A convertible preferred stock	2,898,173	3,368,024
Adjustments to reflect the assumed conversion of Series B convertible preferred stock	—	7,311,165
Adjusted to reflect the assumed exercise of warrants	308,416	389,631
Pro forma weighted-average number of shares outstanding—basic and diluted net loss per share	6,889,774	14,741,705
Pro forma net loss per share—basic and diluted	<u>\$ (0.74)</u>	<u>\$ (0.11)</u>

16. Subsequent Events

The Company has evaluated subsequent events for financial statement purposes occurring through May 30, 2014, the date when these financial statements are available to be issued, and determined that no additional subsequent events had occurred that would require recognition in these financial statements and all material subsequent events that require disclosure have been disclosed.

In April 2014, the Company issued 7,321,003 shares of Series B convertible preferred stock, including 7,025,888 to investors for cash at \$7.53 per share for gross proceeds of \$52.9 million, and 295,115 shares upon the conversion of the 2013 Notes (refer to Note 8). In connection with the closing of the Series B Financing, the Company repurchased 531,208 shares of Series A convertible preferred stock from an investor for \$4.0 million for cash.

In May 2014, the Company entered into a research collaboration and license agreement with Regeneron to discover, develop and commercialize novel gene therapy products for the treatment of ophthalmologic diseases. In addition, Regeneron invested a total of \$4.0 million in the Company's Series B Financing in April 2014, and has the right to purchase up to \$10.0 million of the Company's common stock upon the occurrence of an initial public offering at a price per share equal to the initial public offering price. Under the terms of the agreement, the Company received an initial cash payment including partial payment of license fees, option fees, and collaboration research costs of \$8.0 million. The collaboration covers up to eight distinct therapeutic targets, and Regeneron will have exclusive worldwide rights for each product it moves forward into clinical development. The Company is eligible to receive contingent payments of up to \$80.0 million upon achievement of certain development and regulatory milestones for product candidates directed toward each therapeutic target, for a combined total of up to \$640.0 million in potential milestone payments for product candidates directed toward all eight therapeutic targets, plus a royalty in the low- to mid-single-digits on worldwide net sales of collaboration products. Under the agreement, the Company will collaborate with Regeneron to conduct research for the discovery of novel gene therapy vectors. Subsequent to the filing of an IND with the FDA for a product candidate, Regeneron may exercise its option right to obtain exclusive worldwide rights to further research, develop, and commercialize such product candidates directed to the applicable therapeutic target. For any two therapeutic targets, we have an option to share up to 35% of the worldwide product candidate development costs and profits. As part of the agreement, Regeneron has a time-limited right of first negotiation for certain rights to AVA-101, the Company's gene therapy product currently under development upon completion of the ongoing Phase 2a clinical trial.

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Avalanche Biotechnologies, Inc.

Common Stock

PRELIMINARY PROSPECTUS

Joint Book-Running Managers

**Jefferies
Cowen and Company
Piper Jaffray**

Co-Manager

William Blair & Company

, 2014

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PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution

The following table sets forth the costs and expenses, other than the underwriting discounts and commissions, payable by the registrant in connection with the sale of common stock being registered. All amounts are estimates except for the SEC registration fee, the FINRA filing fee and The NASDAQ Global Market listing fee.

ITEM	AMOUNT TO BE PAID
SEC Registration Fee	\$ 11,997.72
FINRA Filing Fee	12,788
The NASDAQ Global Market Listing Fee	25,000
Printing and Engraving Expenses	350,000
Legal Fees and Expenses	1,200,000
Accounting Fees and Expenses	450,000
Transfer Agent Fees and Expenses	10,000
Miscellaneous Expenses	239,564
Total	<u>\$ 2,300,000</u>

Item 14. Indemnification of Directors and Officers

As permitted by Section 102 of the Delaware General Corporation Law, we have adopted provisions in our amended and restated certificate of incorporation and bylaws that limit or eliminate the personal liability of our directors for a breach of their fiduciary duty of care as a director. The duty of care generally requires that, when acting on behalf of the corporation, directors exercise an informed business judgment based on all material information reasonably available to them. Consequently, a director will not be personally liable to us or our stockholders for monetary damages for breach of fiduciary duty as a director, except for liability for:

- any breach of the director's duty of loyalty to us or our stockholders;
- any act or omission not in good faith or that involves intentional misconduct or a knowing violation of law;
- any act related to unlawful stock repurchases, redemptions or other distributions or payment of dividends; or
- any transaction from which the director derived an improper personal benefit.

These limitations of liability do not affect the availability of equitable remedies such as injunctive relief or rescission. Our amended and restated certificate of incorporation also authorizes us to indemnify our officers, directors and other agents to the fullest extent permitted under Delaware law.

As permitted by Section 145 of the Delaware General Corporation Law, our amended and restated bylaws provide that:

- we may indemnify our directors, officers, employees and agents to the fullest extent permitted by the Delaware General Corporation Law, subject to limited exceptions;
- we may advance expenses to our directors, officers and employees in connection with a legal proceeding to the fullest extent permitted by the Delaware General Corporation Law, subject to limited exceptions; and
- the rights provided in our amended and restated bylaws are not exclusive.

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Our amended and restated certificate of incorporation, attached as Exhibit 3.1 hereto, and our amended and restated bylaws, attached as Exhibit 3.3 hereto, provide for the indemnification provisions described above and elsewhere herein. We intend to enter into separate indemnification agreements with our directors and officers which may be broader than the specific indemnification provisions contained in the Delaware General Corporation Law. These indemnification agreements generally require us, among other things, to indemnify our officers and directors (and under certain circumstances, our directors' affiliated venture capital funds) against liabilities that may arise by reason of their status or service as directors or officers, other than liabilities arising from willful misconduct. These indemnification agreements also generally require us to advance any expenses incurred by the directors or officers as a result of any proceeding against them as to which they could be indemnified. In addition, we have purchased a policy of directors' and officers' liability insurance that insures our directors and officers against the cost of defense, settlement or payment of a judgment in some circumstances. These indemnification provisions and the indemnification agreements may be sufficiently broad to permit indemnification of our officers and directors for liabilities, including reimbursement of expenses incurred, arising under the Securities Act.

The form of Underwriting Agreement, attached as Exhibit 1.1 hereto, provides for indemnification by the underwriters of us and our officers who sign this Registration Statement and directors for specified liabilities, including matters arising under the Securities Act.

Item 15. Recent Sales of Unregistered Securities

The following list sets forth information as to all securities we have sold since January 1, 2011, which were not registered under the Securities Act.

1. We sold an aggregate of 71,875 shares of common stock to employees, directors and consultants for cash consideration in the aggregate amount of \$7.19 upon the exercise of stock options and stock awards.
2. We granted stock options and stock awards to employees, directors and consultants under our Amended and Restated 2006 Equity Incentive Plan covering an aggregate of 3,972,600 shares of common stock, at an average exercise price of \$1.52 per share through July 21, 2014. Of these, options covering 55,000 shares were cancelled without being exercised.
3. In April 2011, we sold an aggregate of 103,434 shares of our Series A convertible preferred stock at a price of \$1.45 per share for an aggregate purchase price of approximately \$149,979 to one accredited investor.
4. In August 2012, we entered into a note purchase agreement pursuant to which we issued unsecured subordinated convertible promissory notes to one accredited investor in an aggregate principal amount of \$2.0 million. In November 2013, the aggregate principal amount and accrued interest on such convertible promissory notes converted into 1,419,959 shares of our Series A convertible preferred stock.
5. In February 2012, we issued warrants to purchase an aggregate of 80,000 shares of our common stock at a price per share of \$0.19 to one accredited investor.
6. In November 2013, we issued 689,655 shares of our Series A convertible preferred stock to one accredited investor at a price per share of \$1.45 for an aggregate purchase price of approximately \$1.0 million.
7. In January and April 2014, we issued unsecured subordinated convertible promissory notes to one accredited investor in an aggregate principal amount of \$2.0 million. In April 2014, the aggregate principal amount on such convertible promissory notes converted into 295,115 shares of our Series B convertible preferred stock.
8. In March 2014, we issued warrants to purchase an aggregate of 25,000 shares of our common stock at a price per share of \$2.75 to one accredited investor.
9. In April 2014, we repurchased an aggregate of 531,208 shares of our Series A convertible preferred stock from one accredited investor at a price per share of \$7.53 for an aggregate purchase price of approximately \$4.0 million.

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10. In April 2014, we sold an aggregate of 7,321,003 shares of our Series B convertible preferred stock for \$55 million, which included conversion of the aggregate principal amount on convertible promissory notes described above, to 45 accredited investors.
11. In May 2014, we issued warrants to purchase an aggregate of 63,415 shares of our common stock at a price per share of \$6.83 to one accredited investor.

We claimed exemption from registration under the Securities Act for the sales and issuances of securities in the transactions described in paragraphs (1) and (2) above under Rule 701 promulgated under the Securities Act, in that they were offered and sold either pursuant to written compensatory plans or pursuant to a written contract relating to compensation, as provided by Rule 701 and for the transactions described in paragraphs (3) through (11) above under Section 4(a)(2) of the Securities Act in that such sales and issuances did not involve a public offering.

Item 16. Exhibits and Financial Statement Schedules**(a) Exhibits**

See the Exhibit Index attached to this Registration Statement, which is incorporated by reference herein.

(b) Financial Statement Schedules

Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the consolidated financial statements or notes thereto.

Item 17. Undertakings

The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned registrant hereby undertakes that:

1. For purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.
2. For the purpose of determining any liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

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[Table of Contents](#)**SIGNATURES**

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant has duly caused this Amendment No. 6 to Registration Statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in Menlo Park, California, on July 30, 2014.

AVALANCHE BIOTECHNOLOGIES, INC.

By: /s/ Thomas W. Chalberg, Jr., Ph.D.
Thomas W. Chalberg, Jr., Ph.D.
President and Chief Executive Officer

Pursuant to the requirements of the Securities Act, this Amendment No. 6 to this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

SIGNATURE	TITLE	DATE
<u>/s/ Thomas W. Chalberg, Jr., Ph.D.</u> Thomas W. Chalberg, Jr., Ph.D.	Director, President and Chief Executive Officer (<i>Principal Executive Officer</i>)	July 30, 2014
<u>/s/ Linda C. Bain</u> Linda C. Bain	Chief Financial Officer (<i>Principal Financial and Accounting Officer</i>)	July 30, 2014
<u>*</u> Mark S. Blumenkranz, M.D.	Chairman of the Board	July 30, 2014
<u>*</u> John P. McLaughlin	Director	July 30, 2014
<u>*</u> Steven D. Schwartz, M.D.	Director	July 30, 2014
<u>*</u> Paul D. Wachter	Director	July 30, 2014

* By: /s/ Linda C. Bain
Attorney-in-Fact

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EXHIBIT INDEX

EXHIBIT NUMBER	DESCRIPTION
1.1**	Form of Underwriting Agreement.
3.1**	Amended and Restated Certificate of Incorporation, as currently in effect.
3.2**	Form of Amended and Restated Certificate of Incorporation, to be in effect upon completion of this offering.
3.3**	Bylaws, as currently in effect.
3.4**	Form of Amended and Restated Bylaws, to be in effect upon completion of the offering.
4.1**	Form of Common Stock Certificate.
4.2**	Form of Warrant to Purchase Shares of Common Stock, issued to Lions Eye Institute.
4.3**	Form of Warrant to Purchase Shares of Common Stock, issued to Cowen and Company, LLC, dated May 15, 2014.
4.4**	Form of Warrant to Purchase Series A Preferred Stock.
4.5**	Amended and Restated Investor Rights Agreement, dated as of April 16, 2014, between Avalanche Biotechnologies, Inc. and certain of its stockholders.
4.6**	Right of First Refusal and Co-Sale Agreement, dated as of April 16, 2014, between Avalanche Biotechnologies, Inc. and certain of its stockholders.
4.7**	Amended and Restated Voting Agreement, dated as of April 16, 2014, between Avalanche Biotechnologies, Inc. and certain of its stockholders.
5.1**	Opinion of Latham & Watkins LLP.
10.1†**	Exclusive License for Use of Recombinant Gene Delivery Vectors for Treating or Preventing Diseases of the Eye, dated as of May 27, 2010, by and between Avalanche Biotechnologies, Inc. and The Regents of the University of California.
10.2†**	Amendment #1 to: Exclusive License for Use of Recombinant Gene Delivery Vectors for Treating or Preventing Diseases of the Eye, effective as of September 17, 2013, by and between Avalanche Biotechnologies, Inc. and The Regents of the University of California.
10.3†**	Research Collaboration and License Agreement, dated as of May 1, 2014, by and between Avalanche Biotechnologies, Inc. and Regeneron Pharmaceuticals, Inc.
10.4***	Amended and Restated 2006 Equity Incentive Plan.
10.5***	Form of 2014 Equity Incentive Award Plan.
10.6***	Form of 2014 Employee Stock Purchase Plan.
10.7***	Letter Agreement, dated as of September 18, 2010, by and between Avalanche Biotechnologies, Inc. and Thomas W. Chalberg, Jr., Ph.D.
10.8***	Letter Agreement, dated as of April 2, 2014, by and between Avalanche Biotechnologies, Inc. and Linda C. Bain.
10.9***	Letter Agreement, dated as of July 15, 2012, by and between Avalanche Biotechnologies, Inc. and Hans P. Hull.
10.10***	Letter Agreement, dated as of June 3, 2013, by and between Avalanche Biotechnologies, Inc. and Mehdi Gasmi.
10.11**	Lease Agreement, dated as of December 20, 2013, by and between Avalanche Biotechnologies, Inc. and O'Brien Drive Portfolio, LLC.
10.12**	Form of Indemnification Agreement for directors and executive officers.
10.13**	2012 Change in Control Benefit Plan.
10.14**	Form of Change in Control Severance Agreement.

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<u>EXHIBIT NUMBER</u>	<u>DESCRIPTION</u>
10.15#**	Form of Chief Executive Officer Change in Control Severance Agreement.
10.16#**	Form of Stock Option Grant Notice and Stock Option Agreement under the Amended and Restated 2006 Equity Incentive Plan.
10.17#**	Form of Stock Option Grant Notice and Stock Option Agreement under the 2014 Equity Incentive Award Plan.
10.18#**	Form of Restricted Stock Award Grant Notice and Restricted Stock Award Agreement under the 2014 Equity Incentive Award Plan.
10.19#**	Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement under the 2014 Equity Incentive Award Plan.
23.1	Consent of independent registered public accounting firm.
23.2**	Consent of Latham & Watkins LLP (included in Exhibit 5.1).
24.1**	Power of Attorney.

† Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment and this exhibit has been filed separately with the SEC.

Indicates management contract or compensatory plan.

** Previously filed.

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Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the use in this Amendment No. 6 to Registration Statement No. 333-197133 of our report dated May 30, 2014 relating to the consolidated financial statements of Avalanche Biotechnologies, Inc. and its subsidiary (collectively, the "Company") as of and for the years ended December 31, 2013 and 2012, and for the period from July 17, 2006 (date of inception) to December 31, 2013 (which report expresses an unqualified opinion on the consolidated financial statements and includes an explanatory paragraph referring to the Company being in the development stage as of December 31, 2013) appearing in the Prospectus, which is part of such Registration Statement, and to the reference to us under the heading "Experts" in such Prospectus.

/s/ Deloitte & Touche LLP

San Jose, California
July 29, 2014